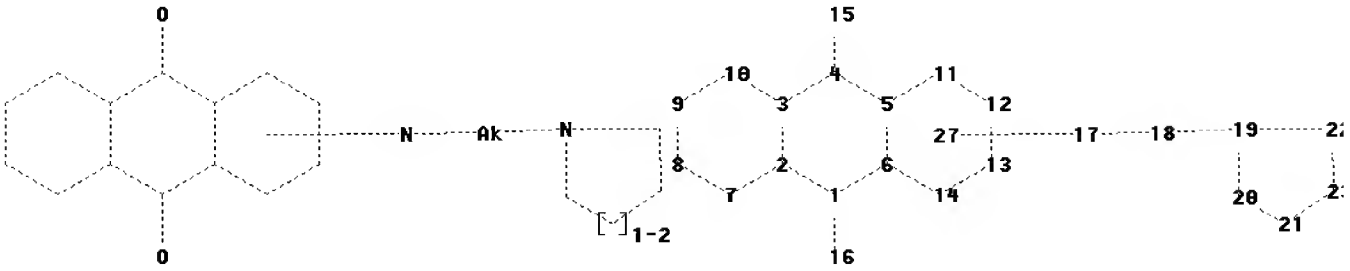
Structures uploaded into STN REGISTRY

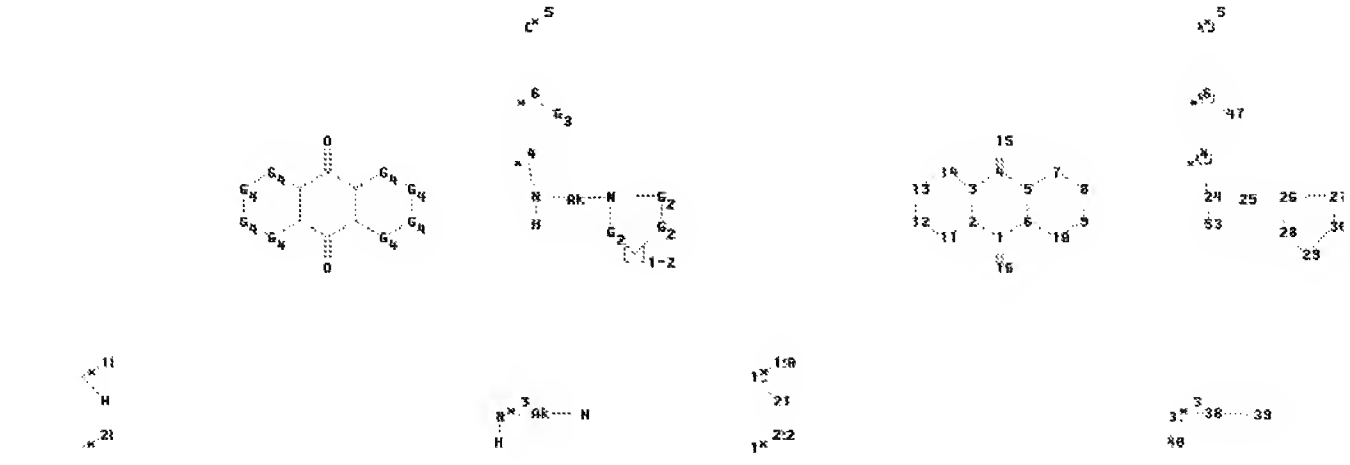
Uploading L1b.str



chain nodes :
15 16 17 18
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 19 20 21 22 23
chain bonds :
1-16 4-15 17-18 18-19
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 5-11 6-14 7-8 8-9 9-10 11-12 12-13
13-14 19-20 19-22 20-21 21-23 22-23
exact/norm bonds :
1-2 1-6 1-16 2-3 2-7 3-4 3-10 4-5 4-15 5-6 5-11 6-14 7-8 8-9 9-10
11-12 12-13 13-14 17-18 18-19 19-20 19-22 20-21 21-23 22-23

Connectivity :
15:1 E exact RC ring/chain 16:1 E exact RC ring/chain
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:Atom
20:Atom 21:Atom
22:Atom 23:Atom 27:CLASS

Uploading L10b.str



chain nodes :
15 16 18 19 20 21 22 23 24 25 37 38 39 40 43 44 45 47 53
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 26 27 28 29 30
chain bonds :
1-16 4-15 18-20 18-21 19-22 19-23 24-25 24-45 24-53 25-26 37-38 37-40
38-39 44-47
ring bonds :
1-2 1-6 2-3 2-11 3-4 3-14 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 12-13
13-14 26-27 26-28 27-30 28-29 29-30
exact/norm bonds :
1-2 1-6 1-16 2-3 2-11 3-4 3-14 4-5 4-15 5-6 5-7 6-10 7-8 8-9 9-10
11-12 12-13 13-14 18-20 18-21 19-22 19-23 24-25 24-45 24-53 25-26 26-27
26-28 28-29 29-30
37-38 37-40 38-39 44-47
exact bonds :
27-30
isolated ring systems :
containing 26 :

G1:O,X,Ak

G2:[*1],[*2]

G3:O,X,Ak,[*3]

G4:[*4],[*5],[*6]

Connectivity :
25:2 E exact RC ring/chain 38:2 E exact RC ring/chain 43:2 E exact RC ring/chain
44:3 E exact RC ring/chain 45:3 E exact RC ring/chain
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS
23:CLASS 24:CLASS 25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 37:CLASS
38:CLASS
39:CLASS 40:CLASS 43:CLASS 44:CLASS 45:CLASS 47:CLASS 53:CLASS

Databases searched

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FILE COVERS 1907 - 27 Aug 2008  VOL 149 ISS 9
FILE LAST UPDATED: 26 Aug 2008  (20080826/ED)

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2008.

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 This file contains CAS Registry Numbers for easy and accurate
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Structure search history

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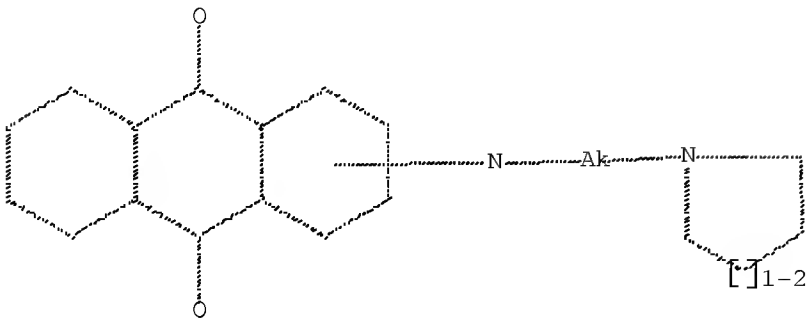


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L10             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
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L15          34 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14
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Structure search results

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L15 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:640230 HCAPLUS Full-text
DOCUMENT NUMBER: 149:9894
TITLE: Preparation of N-oxides of cytotoxic heterocyclylalkylaminoanthraquinones as hypoxia-targeting prodrugs in cancer treatment
INVENTOR(S): Pors, Klaus; Phillips, Roger M.; Patterson, Laurence H.
PATENT ASSIGNEE(S): Somanta Limited, UK
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008062252	A1	20080529	WO 2006-IB3389	20061121

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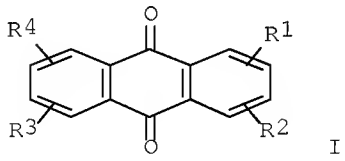
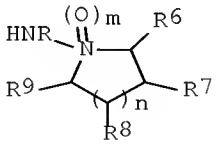
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2006-IB3389 20061121
OTHER SOURCE(S): MARPAT 149:9894
ED Entered STN: 29 May 2008
GI



I

Q1 =

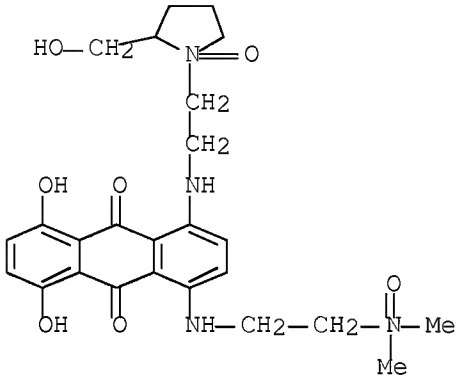


AB Title compds. e.g. [I; R1-R4 = H, alkyl, halo, OH, alkoxy, aryloxy, acyloxy, NRN(R5)2; R = alkylene; R5 = H, (substituted) alkyl, Q1; ≥1 of R6-R8 = X2, X2-substituted alkyl, the others = H, alkyl; R9 = H, alkyl, X2, X2-substituted alkyl; X2 = halo, OH, alkoxy, aryloxy, acyloxy; ≥1 of R1-R4 = Q1; m = 0, 1; n = 1, 2], were prepared for targeting the hypoxic interior of a cell mass followed by in situ reduction and DNA binding. Thus, title compound 1-[[2-(3-chloropiperidin-1-yl-N- oxide)ethyl]amino]-4-[[(2-dimethylamino-N-oxide)ethyl]amino]-5,8- dihydroxyathracene-9,10-dione (CAQ167MN) was prepared

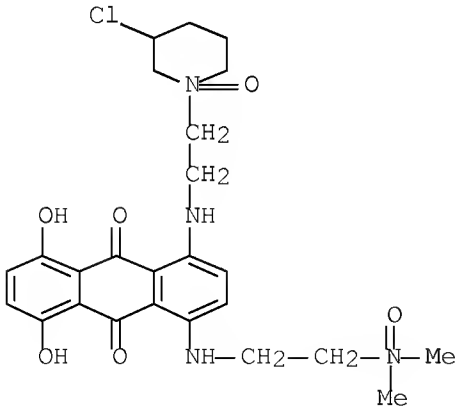
in 62% yield by MCPBA oxidation of the corresponding amine. The title N-oxides penetrated spheroids of HT29 cells and were absent from outer layers of the spheroids.

IT 857637-53-7P 857637-54-8P 857637-55-9P
857637-56-0P 857637-57-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-oxides of cytotoxic heterocyclylalkylaminoanthraquinones as hypoxia-targeting prodrugs in cancer treatment)

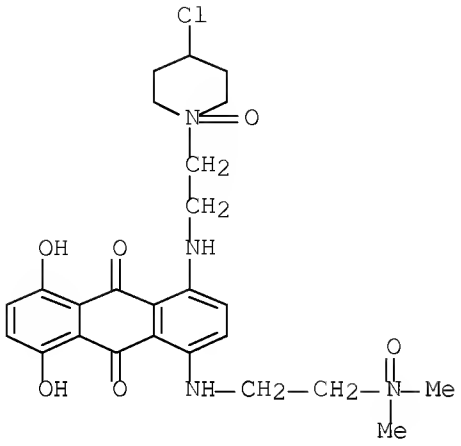
RN 857637-53-7 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(dimethyloxidoamino)ethyl]amino]-5,8-dihydroxy-4-[[2-[2-(hydroxymethyl)-1-oxido-1-pyrrolidinyl]ethyl]amino]- (CA INDEX NAME)



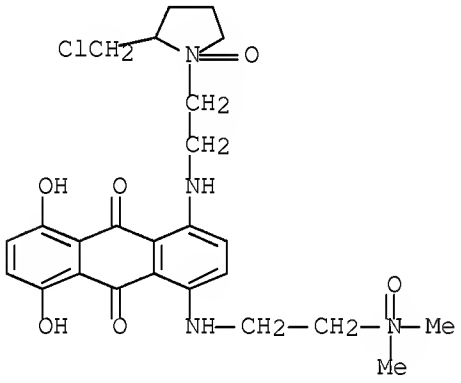
RN 857637-54-8 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(3-chloro-1-oxido-1-piperidinyl)ethyl]amino]-4-[[2-(dimethyloxidoamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



RN 857637-55-9 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(4-chloro-1-oxido-1-piperidinyl)ethyl]amino]-4-[[2-(dimethyloxidoamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



RN 857637-56-0 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[2-(chloromethyl)-1-oxido-1-pyrrolidinyl]ethyl]amino]-4-[[2-(dimethyloxidoamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



RN 857637-57-1 HCAPLUS
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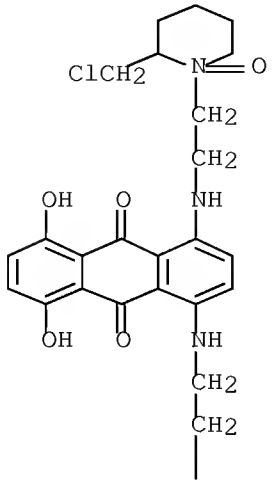
PAGE 1-A



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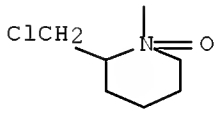

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919488-00-9P 919488-02-1P 938156-36-6P
1029698-93-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-oxides of cytotoxic heterocyclylalkylaminoanthraquinones as hypoxia-targeting prodrugs in cancer treatment)

RN 70945-59-4 HCAPLUS

CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

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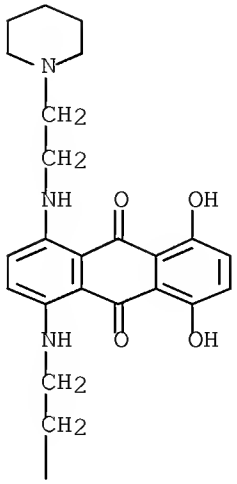

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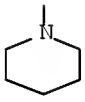

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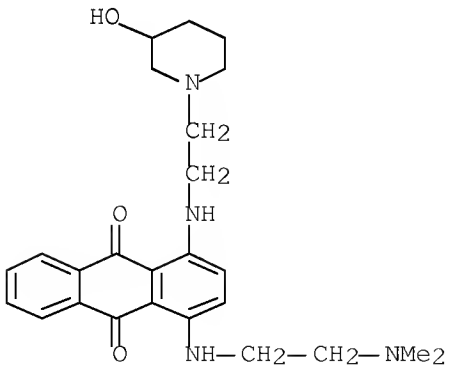

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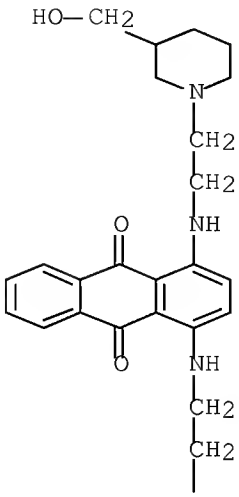
PAGE 1-A



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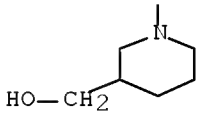

RN 857637-11-7 HCAPLUS
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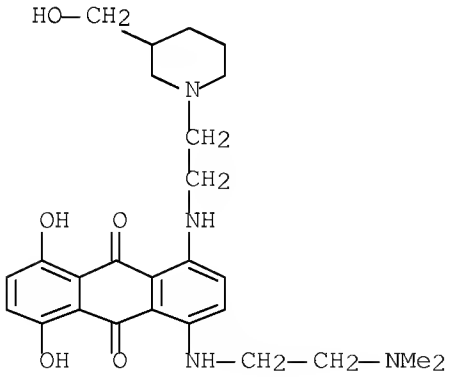

RN 857637-12-8 HCAPLUS
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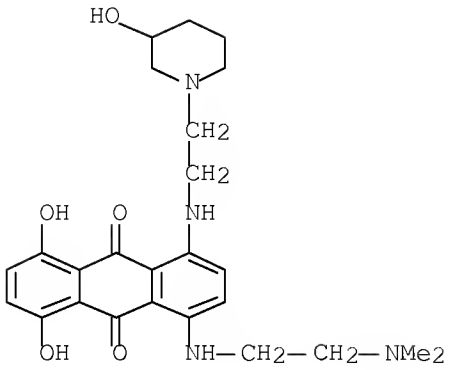

RN 857637-13-9 HCAPLUS
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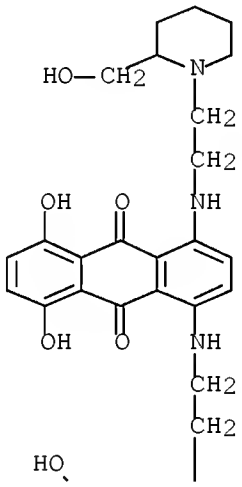

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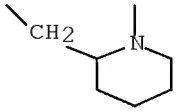

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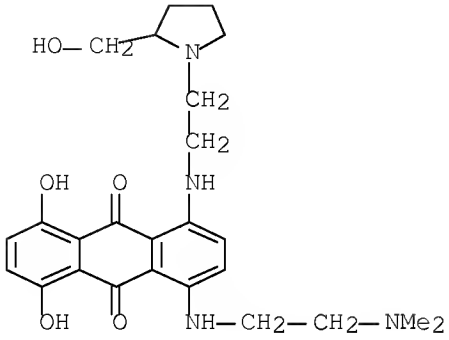

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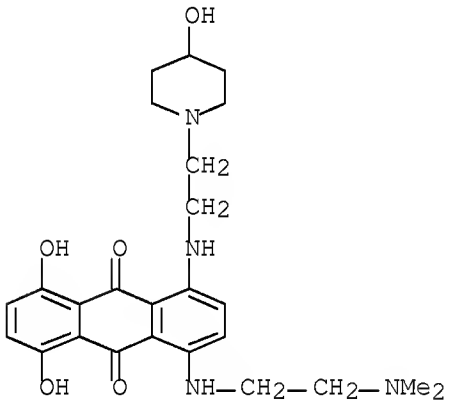

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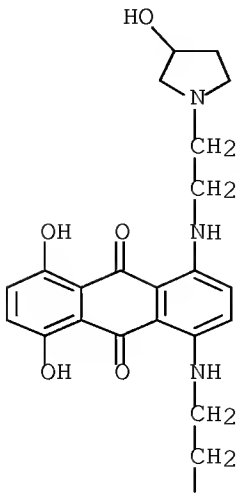
PAGE 1-A



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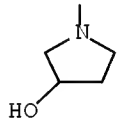

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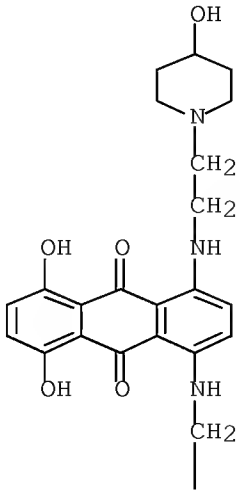
PAGE 1-A



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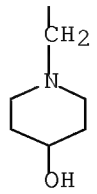

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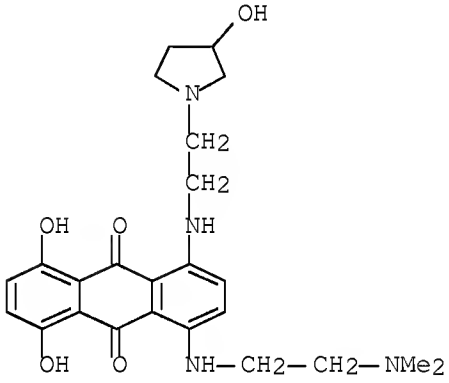

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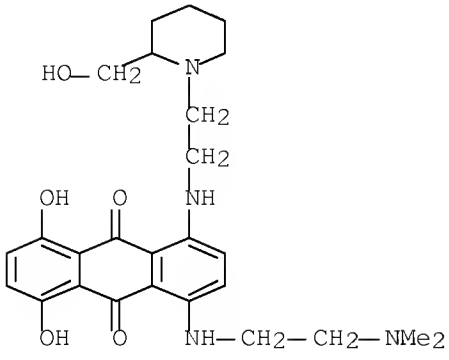

RN 857637-21-9 HCAPLUS
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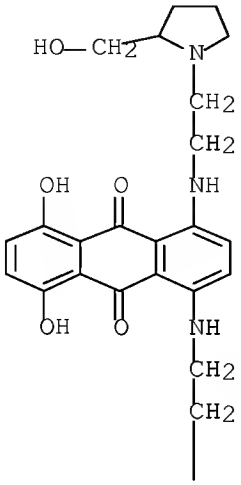

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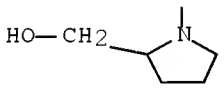
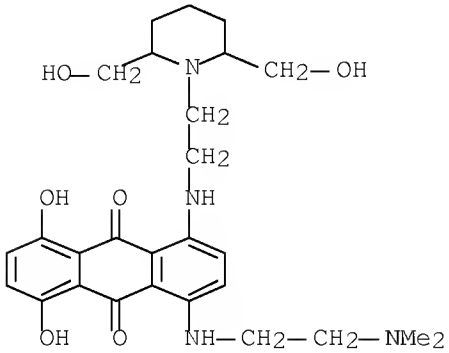
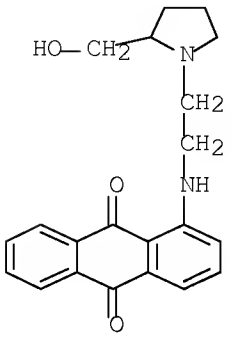


RN 857637-22-0 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[2,6-bis(hydroxymethyl)-1-piperidinyl]ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



RN 857637-23-1 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[2-(hydroxymethyl)-1-pyrrolidinyl]ethyl]amino]-
(CA INDEX NAME)



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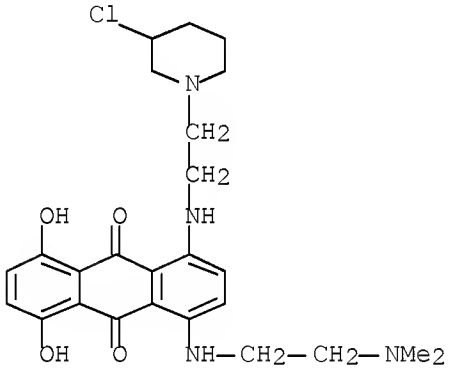

RN 857637-28-6 HCAPLUS
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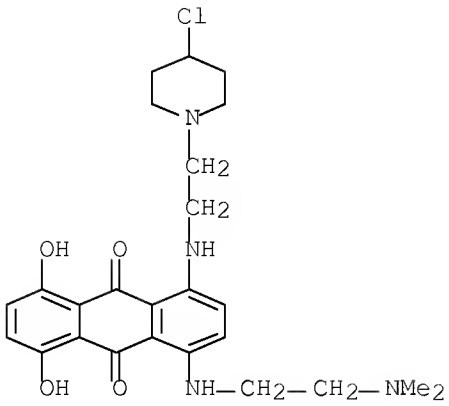

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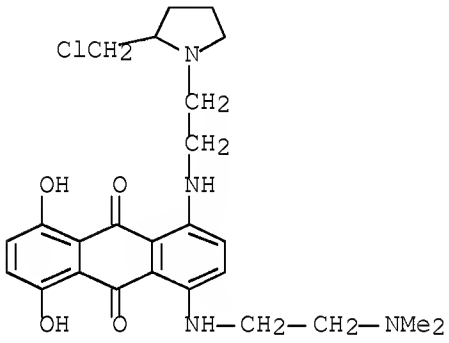

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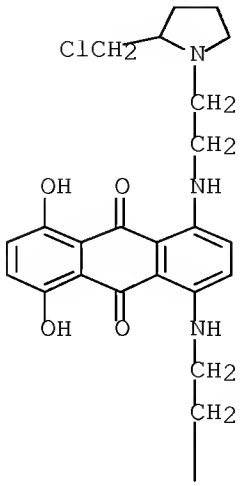

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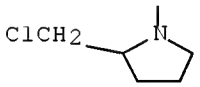

RN 857637-47-9 HCAPLUS
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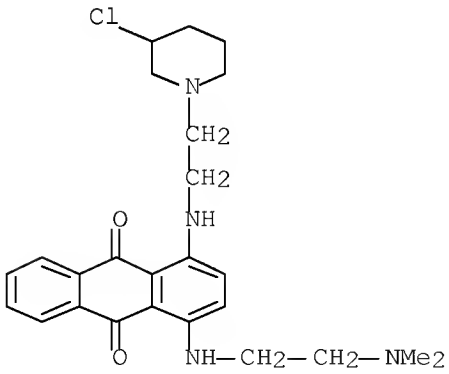

RN 857637-49-1 HCAPLUS
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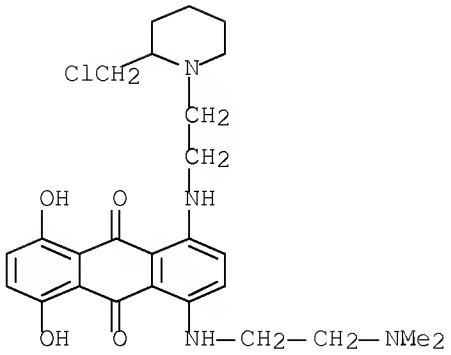

RN 857637-50-4 HCAPLUS
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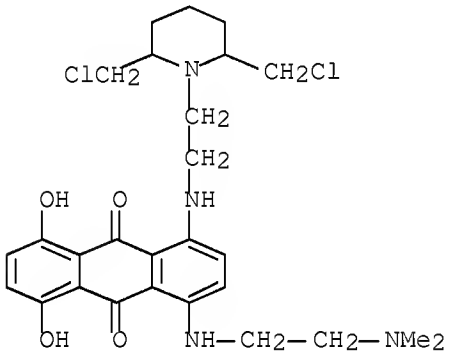

RN 857637-51-5 HCAPLUS
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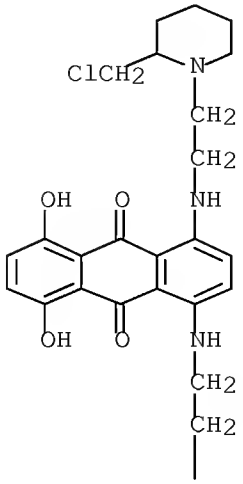

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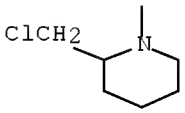

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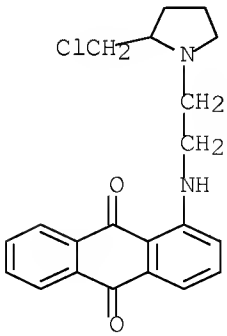

RN 857637-58-2 HCAPLUS
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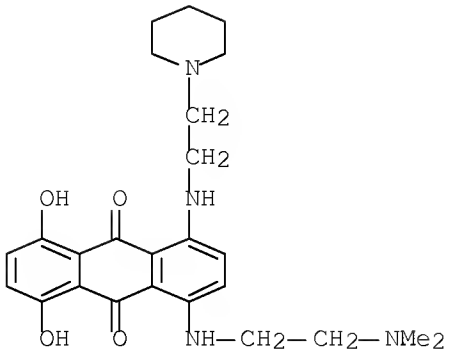

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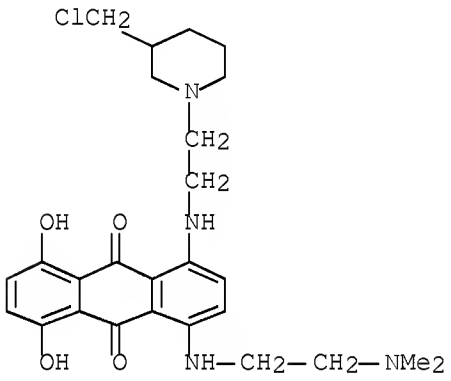

RN 919487-89-1 HCAPLUS
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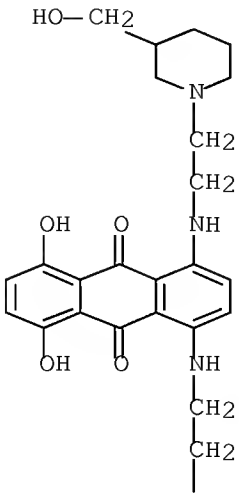

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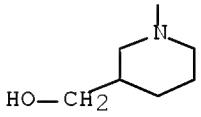

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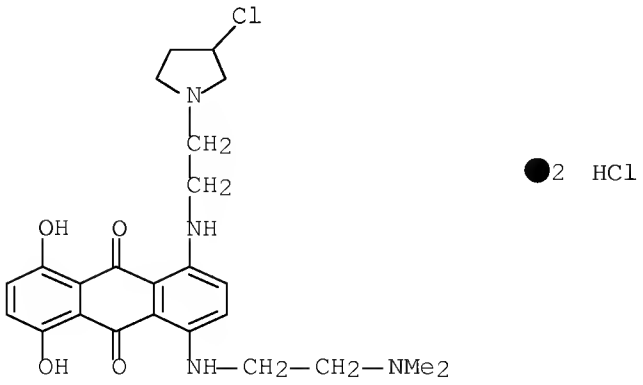

RN 919488-02-1 HCAPLUS
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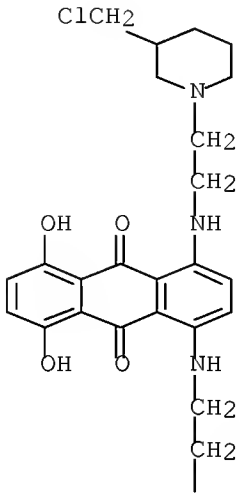
NAME)

PAGE 1-A



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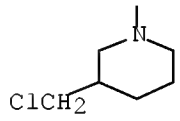

●2 HCl

RN 938156-36-6 HCAPLUS
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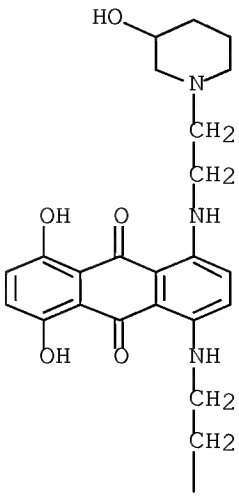

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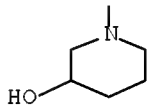

RN 1029698-93-8 HCAPLUS
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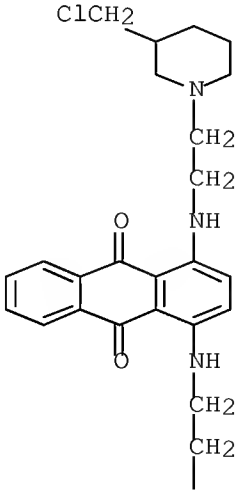

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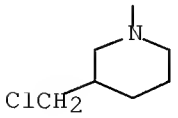

●2 HCl

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1246898 HCAPLUS Full-text
DOCUMENT NUMBER: 146:162991
TITLE: Synthesis of DNA-Directed Pyrrolidinyl and Piperidinyl Confined Alkylating Chloroalkylaminoanthraquinones: Potential for Development of Tumor-Selective N-Oxides
AUTHOR(S): Pors, Klaus; Shnyder, Steven D.; Teesdale-Spittle, Paul H.; Hartley, John A.; Zloh, Mire; Searcey, Mark; Patterson, Laurence H.
CORPORATE SOURCE: Institute of Cancer Therapeutics, University of Bradford, West Yorkshire, BD7 1DP, UK
SOURCE: Journal of Medicinal Chemistry (2006), 49(24), 7013-7023
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:162991
ED Entered STN: 30 Nov 2006
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A novel series of 1,4-disubstituted chloroethylaminoanthraquinones, containing alkylating chloroethylamino functionalities as part of a rigid piperidinyl or pyrrolidinyl ring-system, have been prepared The target compds. were prepared by ipso-displacement of halides of various anthraquinone chromophores by either hydroxylated or chlorinated piperidinyl- or pyrrolidinylalkylamino side chains. The chloroethylaminoanthraquinones were shown to alkylate guanine residues of linearized pBR322 (1-20 μM), and two sym. 1,4-disubstituted anthraquinones (I, n = 1, 2) were shown to interstrand cross-link DNA in the low nM range. Several 1,4-disubstituted chloroethylaminoanthraquinones were potently cytotoxic (IC50 values: ≤40 nM) in human ovarian cancer A2780 cells. Two agents (II, NR1R2 = 2-chloromethylpyrrolidino, 3-chloropiperidino) exhibited mean GI50 values of 96 nM and 182 nM, resp., in the NCI human tumor cell line panel. Derivatization of the potent DNA crosslinking agent I [n = 2]

to an N-oxide resulted in loss of the DNA unwinding, DNA interstrand crosslinking and cytotoxic activity of the parent mol.

IT 857637-13-9
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation of DNA-directed pyrrolidinyl and piperidinyl confined alkylating chloroalkylaminoanthraquinones)

RN 857637-13-9 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-[2-(hydroxymethyl)-1-piperidinyl]ethyl]amino]- (CA INDEX NAME)

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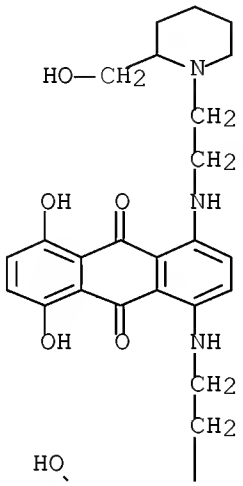

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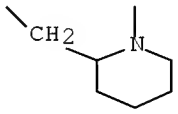

IT 857637-23-1P 919487-89-1P 919487-91-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of DNA-directed pyrrolidinyl and piperidinyl confined alkylating chloroalkylaminoanthraquinones)

RN 857637-23-1 HCAPLUS
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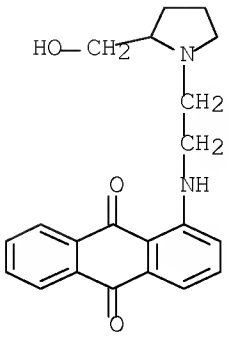

RN 919487-89-1 HCAPLUS
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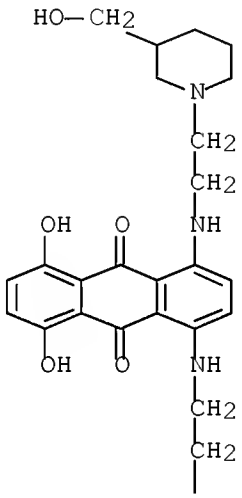

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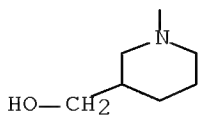

RN 919487-91-5 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis[[2-[2-(chloromethyl)-1-piperidinyl]ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)

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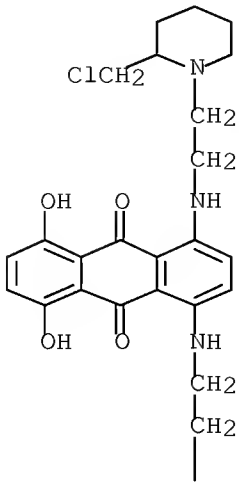

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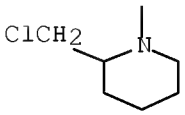

●2 HCl

IT 70945-59-4P 857637-52-6P 857637-57-1P
919487-90-4P 919487-92-6P 919487-93-7P
919487-94-8P 919487-99-3P 919488-00-9P
919488-01-0P 919488-02-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of DNA-directed pyrrolidinyl and piperidinyl confined alkylating chloroalkylaminoanthraquinones)
RN 70945-59-4 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

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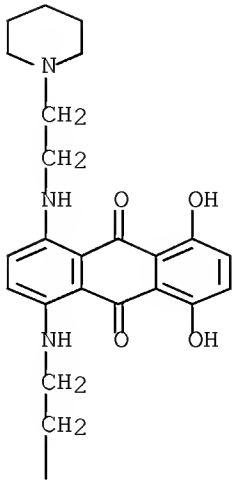

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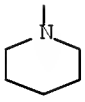

RN 857637-52-6 HCAPLUS
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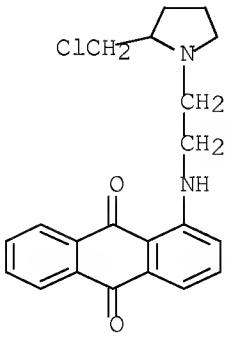
(CA INDEX NAME)



RN 857637-57-1 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis[[2-[2-(chloromethyl)-1-oxido-1-
piperidinyl]ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)

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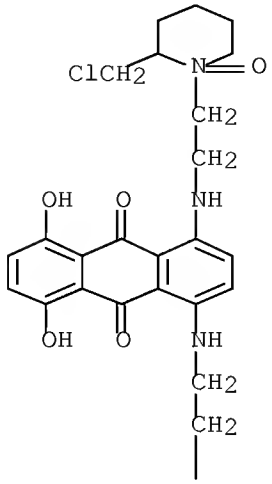

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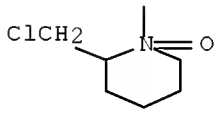
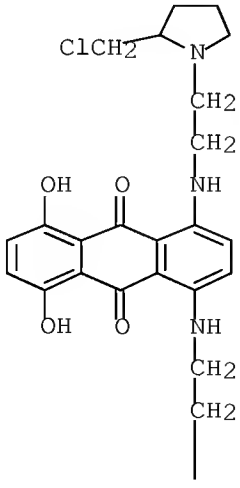
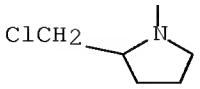


RN 919487-90-4 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis[[2-[2-(chloromethyl)-1-pyrrolidinyl]ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)

PAGE 1-A

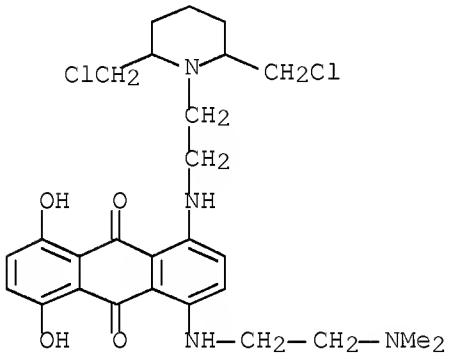


PAGE 2-A



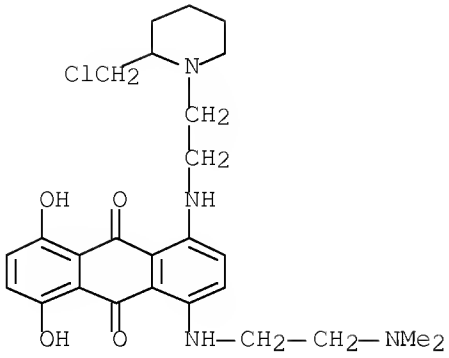
●2 HCl

RN 919487-92-6 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[2,6-bis(chloromethyl)-1-piperidinyl]ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)



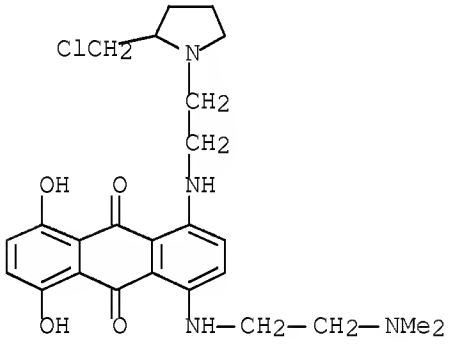
●2 HCl

RN 919487-93-7 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[2-(chloromethyl)-1-piperidinyl]ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)



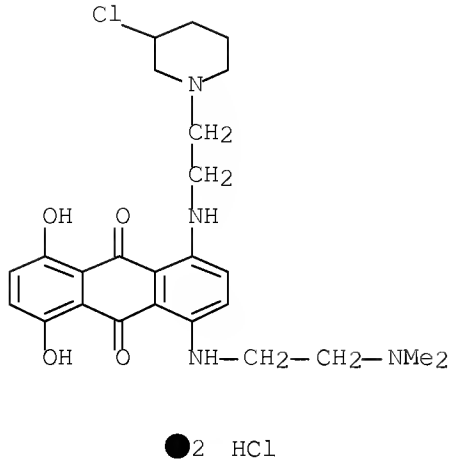
●2 HCl

RN 919487-94-8 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[2-(chloromethyl)-1-pyrrolidinyl]ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)

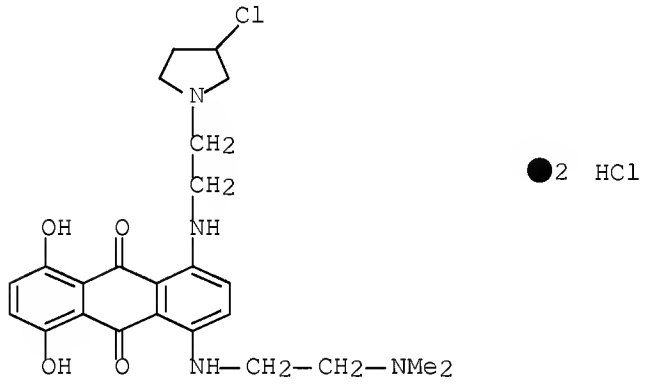


●2 HCl

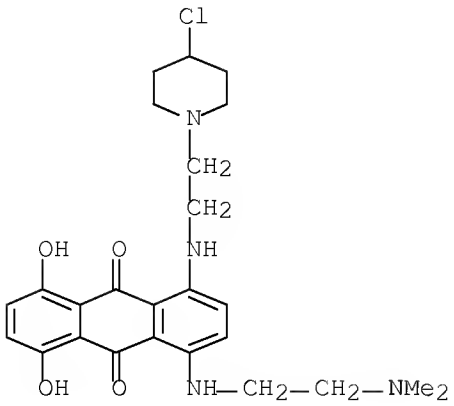
RN 919487-99-3 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(3-chloro-1-piperidinyl)ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)



RN 919488-00-9 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(3-chloro-1-pyrrolidinyl)ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)



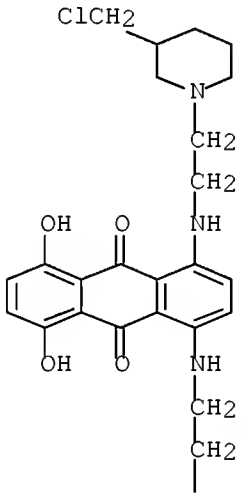
RN 919488-01-0 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(4-chloro-1-piperidinyl)ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)



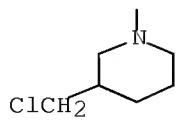
●2 HCl

RN 919488-02-1 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis[[2-[3-(chloromethyl)-1-piperidinyl]ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)

PAGE 1-A



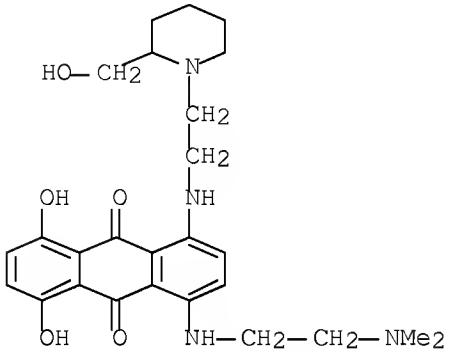
PAGE 2-A



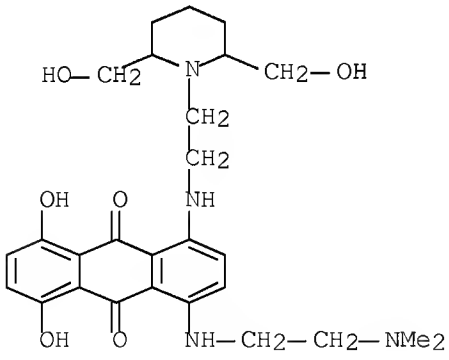
●2 HCl

IT 857637-20-8 857637-22-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of DNA-directed pyrrolidinyl and piperidinyl confined alkylating chloroalkylaminoanthraquinones)

RN 857637-20-8 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-4-[[2-[2-(hydroxymethyl)-1-piperidinyl]ethyl]amino]- (CA INDEX NAME)



RN 857637-22-0 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[2,6-bis(hydroxymethyl)-1-piperidinyl]ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:269917 HCAPLUS Full-text
DOCUMENT NUMBER: 144:311799
TITLE: 5,8-Dihydroxyanthracenedione bis-N-oxide compounds as antiproliferative agents, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Curd, John G.; Capizzi, Robert L.; Keana, John F. W.
PATENT ASSIGNEE(S): Novacea, Inc., USA

SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006031719	A2	20060323	WO 2005-US32398	20050914
WO 2006031719	A3	20060914		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-609253P P 20040914
OTHER SOURCE(S): MARPAT 144:311799
ED Entered STN: 23 Mar 2006
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

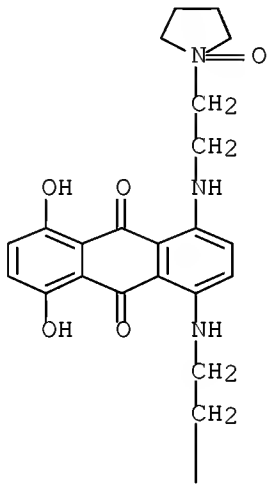
AB The invention relates to anthracenedione compds. having formula I, which are useful as antiproliferative or anti-inflammatory agents. In compds. I, R1 and R2 are independently H, OH, halo, alkyl, alkoxy, aryloxy, carboxy, sulfonyl, etc., or R1 and R2 together form an aryl group; R3 and R4 are independently H or F, or R3 and R4 together form an aryl group; R5 and R6 are independently H, alkyl, or hydroxyalkyl, or R1 and R5 together and/or R2 and R6 together form a ring; R7 and R8 are independently selected from alkyl, hydroxyalkyl, or haloalkyl, or R7 and R8, together with the adjacent nitrogen atom, form a heterocycle; R9 and R10 are independently selected from alkyl, hydroxyalkyl, or haloalkyl, or R9 and R10, together with the adjacent nitrogen atom, form a heterocycle; and A and B are independently selected from (CH2)n, cycloalkyl, or aryl, or form a heterocycle with the two adjacent nitrogen atoms, where n is 1-4; with the provisos that at least one of R1 to R6 is other than H, at least one of R7 to R10 is haloalkyl or R7 and R8 or R9 and R10 form a heterocycle with the adjacent nitrogen atom. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I, optionally including one or more other chemotherapeutic or anti-inflammatory agents, as well as to the use of the compns. for treating, preventing or ameliorating hyperproliferative disorders, such as cancer. Diels-Alder reaction of 2-fluoro-1,4-benzenediol with 3,6-difluorophthalic anhydride followed by dehydration gave trifluoroanthracenedione II, which underwent substitution with N,N-dimethyl-1,2-ethanediamine, N-oxidation, and fluorination with N-fluoropyridinium triflate to give anthracenedione III. The compds. of the invention are active as antiproliferative agents and/or anti-inflammatory agents (no data).

IT 879884-75-0P 879884-77-2P 879884-79-4P
879884-81-8P 879884-83-0P 879884-85-2P

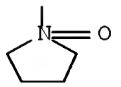
879884-87-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of dihydroxyanthracenedione N-oxides as antiproliferative or anti-inflammatory agents)

RN 879884-75-0 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-oxido-1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A

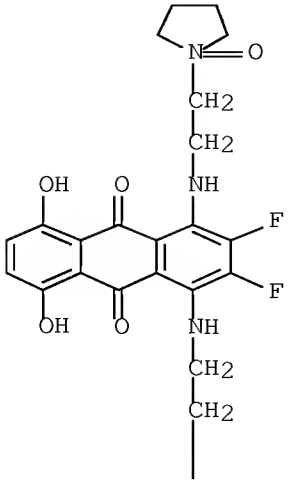


PAGE 2-A



RN 879884-77-2 HCAPLUS
CN 9,10-Anthracenedione, 2,3-difluoro-5,8-dihydroxy-1,4-bis[[2-(1-oxido-1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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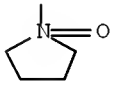
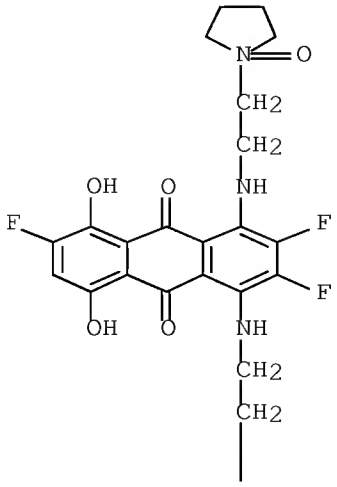


RN 879884-79-4 HCAPLUS
CN 9,10-Anthracenedione, 2,3,6-trifluoro-5,8-dihydroxy-1,4-bis[[2-(1-oxido-1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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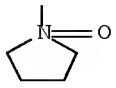
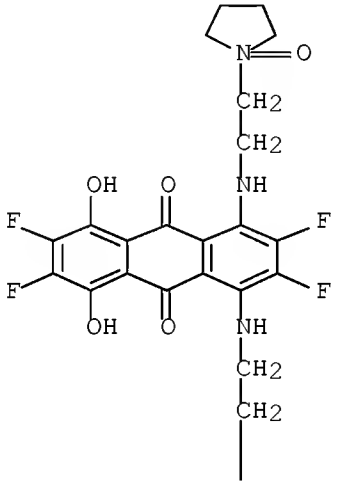


RN 879884-81-8 HCAPLUS
CN 9,10-Anthracenedione, 2,3,6,7-tetrafluoro-1,4-dihydroxy-5,8-bis[[2-(1-oxido-1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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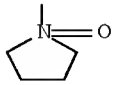
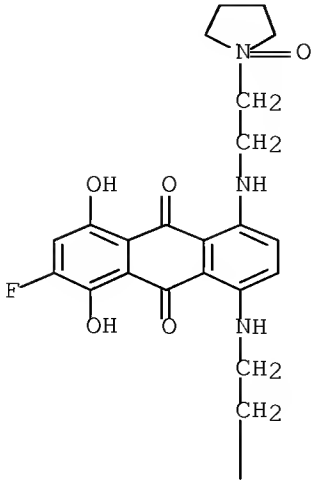


RN 879884-83-0 HCAPLUS
CN 9,10-Anthracenedione, 2-fluoro-1,4-dihydroxy-5,8-bis[[2-(1-oxido-1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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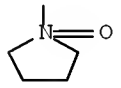
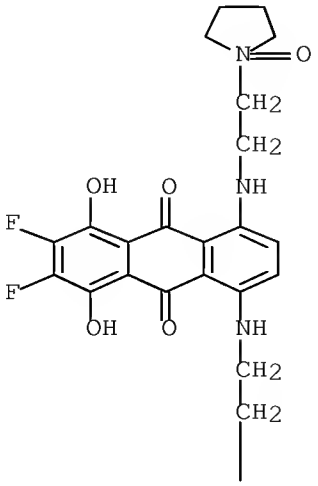


RN 879884-85-2 HCAPLUS
CN 9,10-Anthracenedione, 2,3-difluoro-1,4-dihydroxy-5,8-bis[[2-(1-oxido-1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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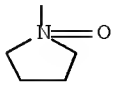
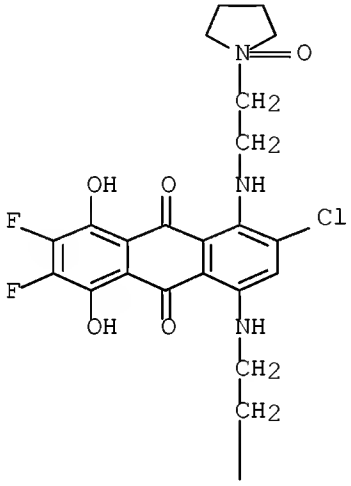


RN 879884-87-4 HCAPLUS
CN 9,10-Anthracenedione, 6-chloro-2,3-difluoro-1,4-dihydroxy-5,8-bis[[2-(1-oxido-1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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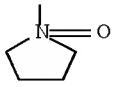
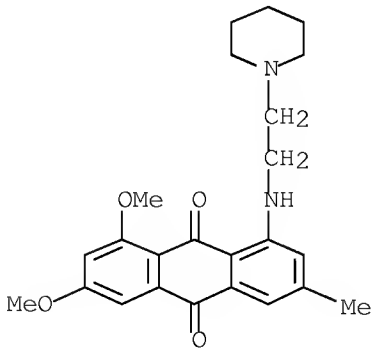
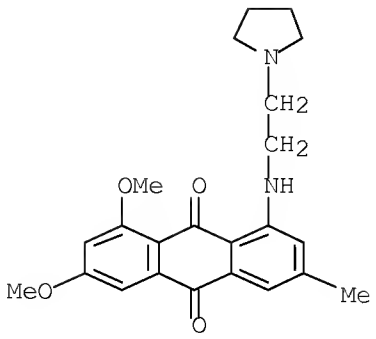


L15 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1030478 HCAPLUS Full-text
DOCUMENT NUMBER: 143:415734
TITLE: Oxidative damage of parental drug-sensitive KB cells and multidrug resistant KBv200 cells mediated by anthraquinone derivatives
AUTHOR(S): Ding, Yan; Liang, Yongju; Lu, Yu; Chen, Liming; Li, Yanfang; Gu, Lianquan; Fu, Liwu

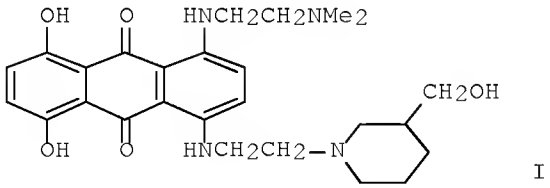
CORPORATE SOURCE: Cancer Center, Sun Yat-Sen University, Guangzhou, Guangdong Province, 510060, Peop. Rep. China
SOURCE: Zhongcaoyao (2004), 35(11), 1259-1262
CODEN: CTYAD8; ISSN: 0253-2670
PUBLISHER: Zhongcaoyao Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
ED Entered STN: 26 Sep 2005
AB Cytotoxicity was determined by tetrazolium (MTT) assay. Reactive oxygen species (ROS) levels and mitochondrial membrane potential ($\Delta\Psi$m in cells resp. labeled by DCFH-DA and DiOC6) were assayed by flow cytometry. All four anthraquinone derivs. suppressed proliferation of KB and KBv200 cells, showed potent cytotoxicity, the mean IC50 of H-19 (1, 8-dimethylaminethylamine-3-methyl-6-methoxy-anthraquinone) to KB and KBv200 cells was 1.37 and 1.42 μmol/L, resp. IC50 of H-21 (1-pyridylethylamine-3-methyl-6,8-dimethoxy-anthraquinone) was 13.0 and 17.9 μmol/L, IC50 of H-25 (1-pyrrolylethylamine-3-methyl-6,8-dimethoxy- anthraquinone) was 8.5 and 11.7 μmol/L, IC50 of H-28 (1-hydroyxlbutylamine-3-methyl-6,8-dimethoxy-anthraquinone) was 7.6 and 8.6 μmol/L. The IC50 of them to multidrug resistant (MDR) KBv200 cells was similar to that of them to the parental drug-sensitive KB cells ($P>0.05$). The generation of ROS increased obviously after the cells were incubated with them for 12 h, the increase of ROS reached the peak after treated for 24 h and the increase of ROS was not obvious after treated for 48 h. The levels of $\Delta\Psi$m were time-dependently decreased after treating with four compds. for 12, 24, and 48 h. The growth of both MDR KBv200 cells and parental drug-sensitive KB cells were inhibited by the treatment of four anthraquinone derivative in vitro. The mechanism of their effects is associated with the increase of the cellular ROS level and the decrease of $\Delta\Psi$m.
IT 868395-48-6 868395-49-7
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxidative damage of parental drug-sensitive KB cells and multidrug resistant KBv200 cells mediated by anthraquinone derivs.)
RN 868395-48-6 HCAPLUS
CN 9,10-Anthracenedione, 1,3-dimethoxy-6-methyl-8-[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)



RN 868395-49-7 HCAPLUS
CN 9,10-Anthracenedione, 1,3-dimethoxy-6-methyl-8-[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)



L15 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1008901 HCAPLUS Full-text
DOCUMENT NUMBER: 143:440042
TITLE: Development of Nonsymmetrical 1,4-Disubstituted Anthraquinones That Are Potently Active against Cisplatin-Resistant Ovarian Cancer Cells
AUTHOR(S): Pors, Klaus; Plumb, Jane A.; Brown, Robert; Teesdale-Spittle, Paul; Searcey, Mark; Smith, Paul J.; Patterson, Laurence H.
CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry, The School of Pharmacy, University of London, London, WC1N 1AX, UK
SOURCE: Journal of Medicinal Chemistry (2005), 48(21), 6690-6695
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:440042
ED Entered STN: 19 Sep 2005
GI



I

AB A novel series of 1,4-disubstituted aminoanthraquinones were prepared by ipso-displacement of 1,4-difluoro-5,8-dihydroxyanthraquinones by hydroxylated piperidinyl- or pyrrolidinylalkylamino side chains. The compds. were evaluated in the A2780 ovarian cancer cell line and its cisplatin-resistant variants (A2780/cp70 and A2780/MCP1). The novel anthraquinones were shown to possess up to 5-fold increased potency against the cisplatin-resistant cells compared to the wild-type cells. Growth curve anal. of the hydroxyethylaminoanthraquinone I in the osteosarcoma cell line U-2 OS showed

that the cell cycle is not frozen, rather there is a late cell cycle arrest consistent with the action of a DNA-damaging topoisomerase II inhibitor. Accumulative apoptotic events, using time lapse photog., indicate that I is capable of fully engaging cell cycle arrest pathways in G2 in the absence of early apoptotic commitment. I and its chloro analog retained significant activity against human A2780/cp70 xenografted tumors in mice.

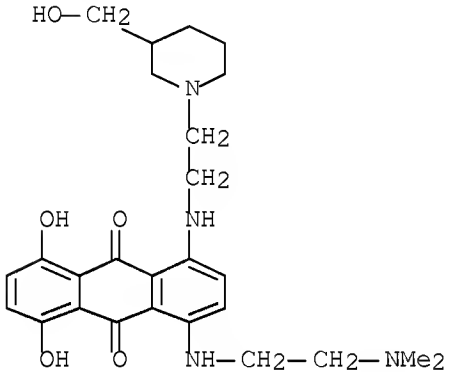
IT 857637-11-7P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(preparation of nonsym. 1,4-disubstituted anthraquinones active against cisplatin-resistant ovarian cancer cells)

RN 857637-11-7 HCAPLUS

CN 9,10-Anthracenedione, 1-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-4-[[2-[3-(hydroxymethyl)-1-piperidinyl]ethyl]amino]- (CA INDEX NAME)



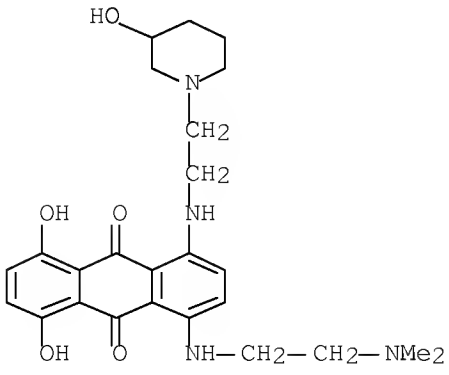
IT 857637-12-8P 857637-15-1P 857637-20-8P
857637-58-2P 868830-16-4P 868830-17-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of nonsym. 1,4-disubstituted anthraquinones active against cisplatin-resistant ovarian cancer cells)

RN 857637-12-8 HCAPLUS

CN 9,10-Anthracenedione, 1-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-4-[[2-(3-hydroxy-1-piperidinyl)ethyl]amino]- (CA INDEX NAME)



RN 857637-15-1 HCAPLUS
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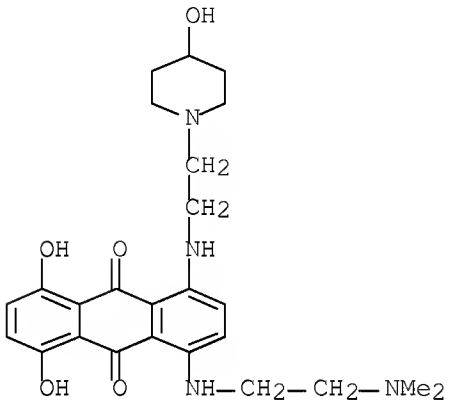
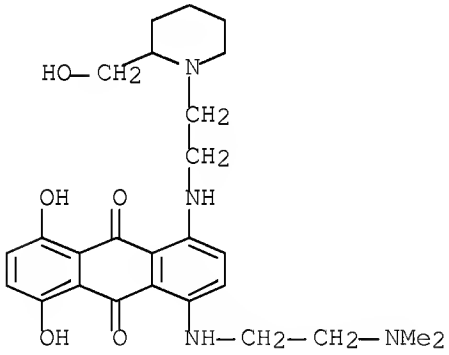


RN 857637-20-8 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-4-[[2-[2-(hydroxymethyl)-1-piperidinyl]ethyl]amino]- (CA INDEX NAME)



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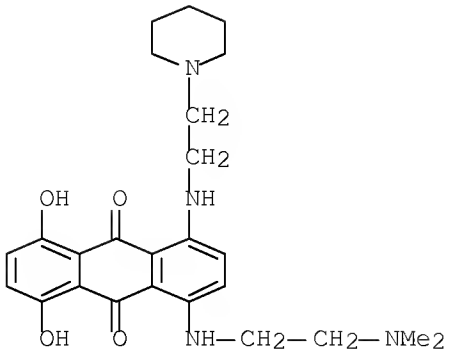
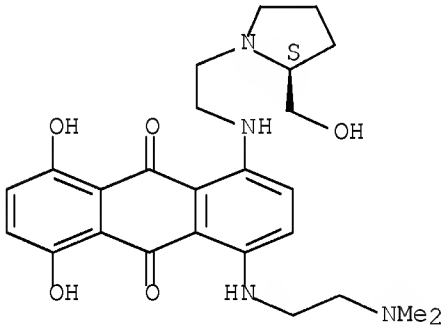
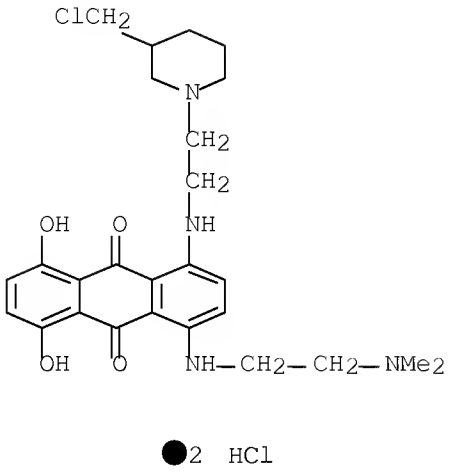


RN 868830-16-4 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-4-[[2-[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]ethyl]amino]- (CA INDEX NAME)

Absolute stereochemistry.



RN 868830-17-5 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[3-(chloromethyl)-1-piperidinyl]ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-, hydrochloride (1:2) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:588893 HCAPLUS Full-text
DOCUMENT NUMBER: 143:115360
TITLE: A preparation of anthraquinone derivatives, useful as antitumor agents
INVENTOR(S): Patterson, Laurence Hylton; Pors, Klaus; Teesdale-Spittle, Paul Henry
PATENT ASSIGNEE(S): School of Pharmacy, University of London, UK
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005061453	A1	20050707	WO 2004-GB5390	20041222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004303592	A1	20050707	AU 2004-303592	20041222
CA 2550839	A1	20050707	CA 2004-2550839	20041222
EP 1701939	A1	20060920	EP 2004-806187	20041222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1934079	A	20070321	CN 2004-80041751	20041222
JP 2007516270	T	20070621	JP 2006-546313	20041222
IN 2006DN03556	A	20070810	IN 2006-DN3556	20060620

US 20080027107 A1 20080131 US 2007-596783 20070208
PRIORITY APPLN. INFO.: GB 2003-29820 A 20031223
GB 2003-30011 A 20031224
WO 2004-GB5390 W 20041222
OTHER SOURCE(S): CASREACT 143:115360; MARPAT 143:115360
ED Entered STN: 08 Jul 2005
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

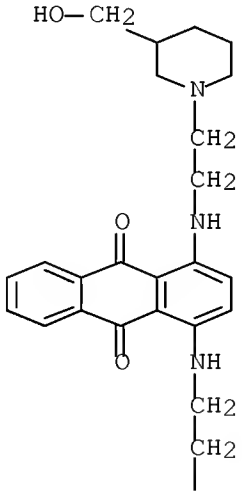
AB The invention relates to a preparation of anthraquinone derivs. of formula I [wherein: R1 to R4 are each selected from H, alkyl, halogen, NH-alkanediyl-heterocycle, or OH, etc.], useful as antitumor agents. For instance, anthraquinone derivative II (inhibition of cell growth: IC50 = 8.4 nM) was prepared via amination of fluoroanthracene derivative III by [1-(2-aminoethyl)piperidin-3-yl]methanol with a yield of 68%.

IT 857637-10-6P 857637-11-7P 857637-13-9P
857637-14-0P 857637-20-8P 857637-22-0P
857637-23-1P 857637-24-2P 857637-28-6P
857637-32-2P 857637-46-8P 857637-51-5P
857637-53-7P 919487-89-1P 938156-36-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of anthraquinone derivs. useful as antitumor agents)

RN 857637-10-6 HCAPLUS

CN 9,10-Anthracenedione, 1,4-bis[[2-[3-(hydroxymethyl)-1-piperidinyl]ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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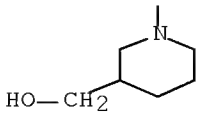

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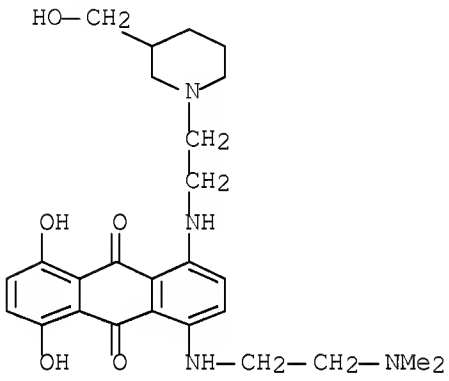
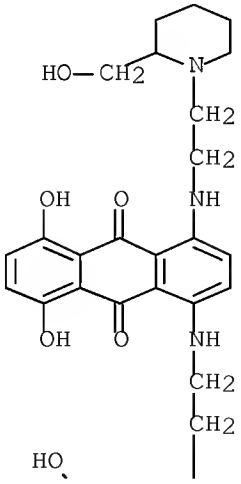
CN 9,10-Anthracenedione, 1-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-4-[[2-[3-(hydroxymethyl)-1-piperidinyl]ethyl]amino]- (CA INDEX NAME)



RN 857637-13-9 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-[2-(hydroxymethyl)-1-piperidinyl]ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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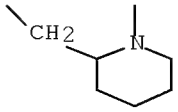
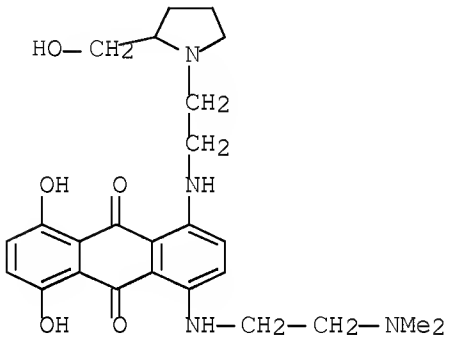


RN 857637-14-0 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-4-[[2-[2-(hydroxymethyl)-1-pyrrolidinyl]ethyl]amino]- (CA INDEX NAME)



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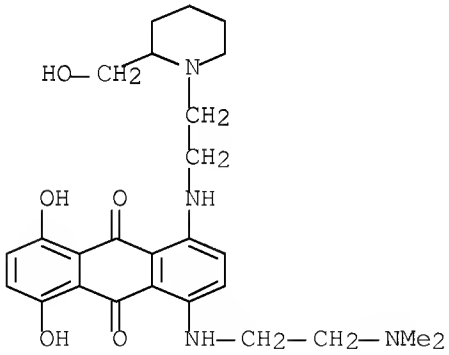

RN 857637-22-0 HCAPLUS
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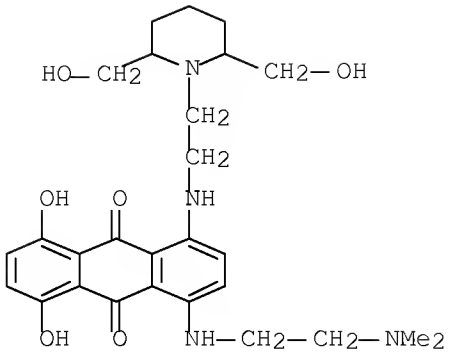

RN 857637-23-1 HCAPLUS
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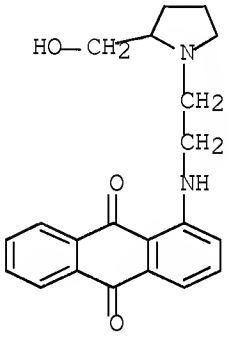
(CA INDEX NAME)



RN 857637-24-2 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(3-chloro-1-piperidinyl)ethyl]amino]-4-[[2-
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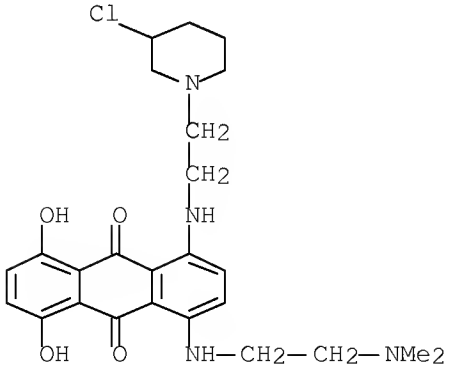

RN 857637-28-6 HCAPLUS

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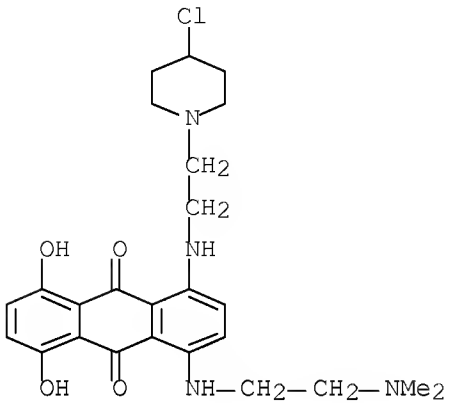
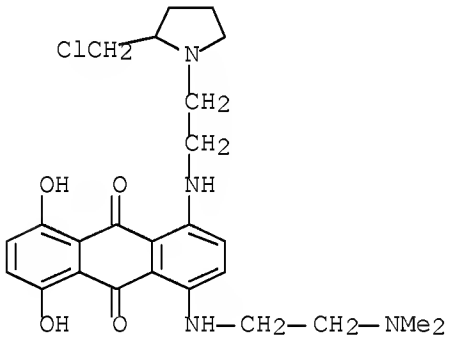


RN 857637-32-2 HCAPLUS

CN 9,10-Anthracenedione, 1-[[2-[2-(chloromethyl)-1-pyrrolidinyl]ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



RN 857637-46-8 HCAPLUS

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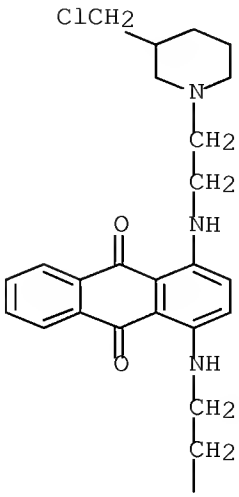
PAGE 1-A



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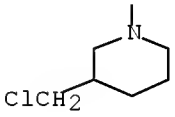

RN 857637-51-5 HCAPLUS
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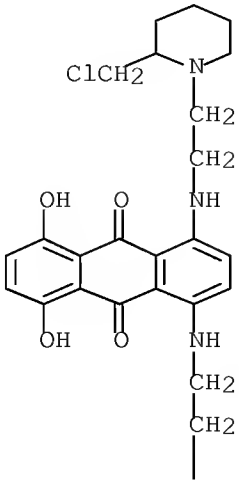
PAGE 1-A



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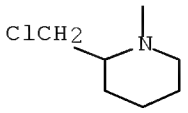
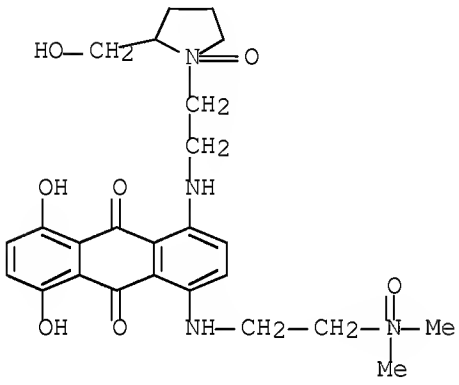


RN 857637-53-7 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(dimethyloxidoamino)ethyl]amino]-5,8-dihydroxy-4-[[2-[2-(hydroxymethyl)-1-oxido-1-pyrrolidinyl]ethyl]amino]- (CA INDEX NAME)



RN 919487-89-1 HCAPLUS
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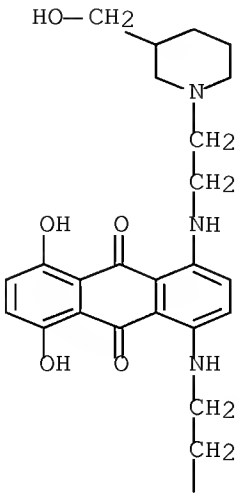
PAGE 1-A



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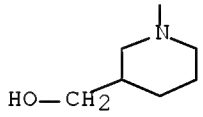

RN 938156-36-6 HCAPLUS
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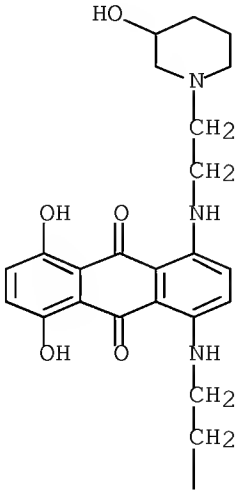
PAGE 1-A



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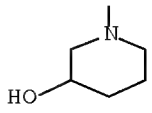

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857637-39-9P 857637-47-9P 857637-48-0P
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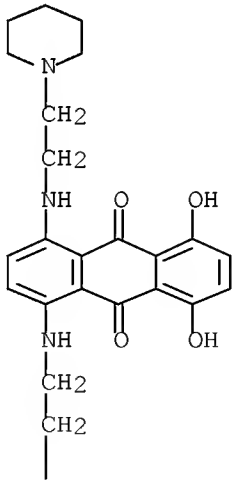
857637-57-1P 857637-58-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of anthraquinone derivs. useful as antitumor agents)

RN 70945-59-4 HCAPLUS

CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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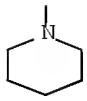

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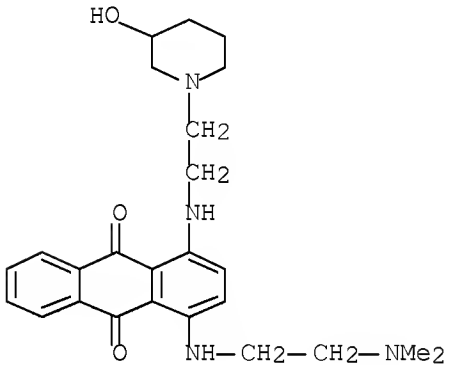

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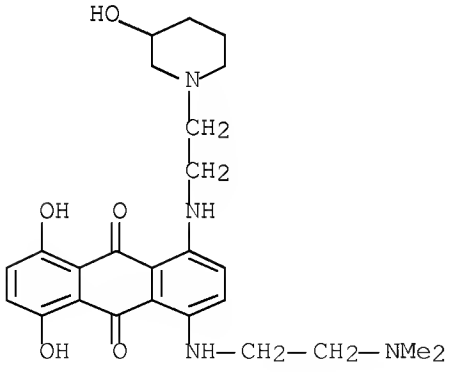

RN 857637-15-1 HCAPLUS
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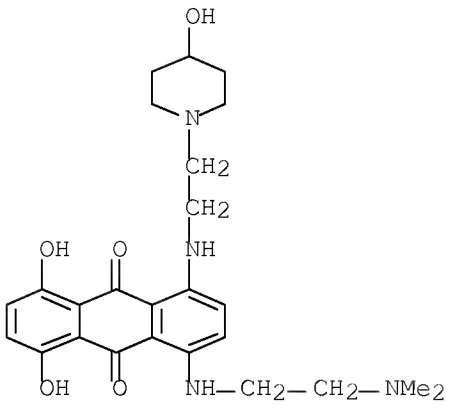
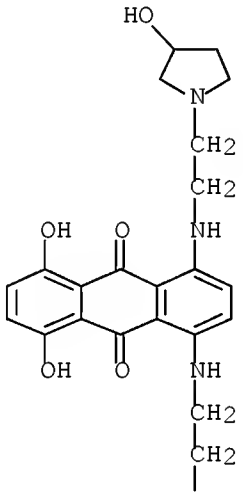
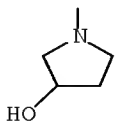


RN 857637-16-2 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(3-hydroxy-1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A

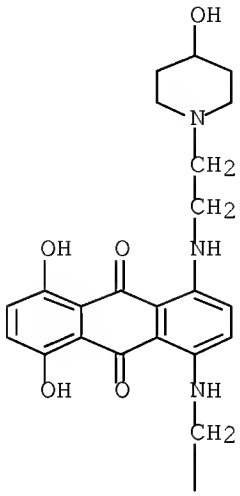


PAGE 2-A

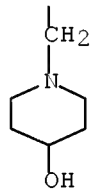


RN 857637-17-3 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(4-hydroxy-1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

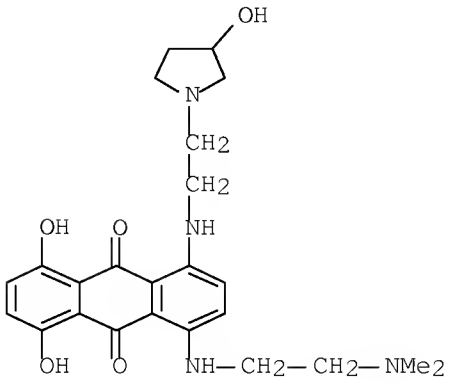
PAGE 1-A



PAGE 2-A

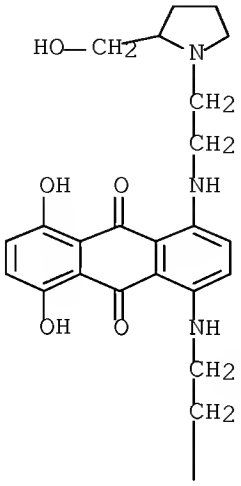


RN 857637-19-5 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-4-[[2-(3-hydroxy-1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)



RN 857637-21-9 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-[2-(hydroxymethyl)-1-pyrrolidinyl]ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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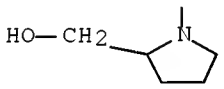

RN 857637-36-6 HCAPLUS
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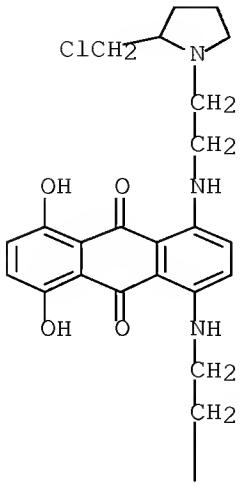
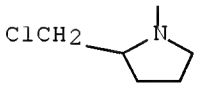
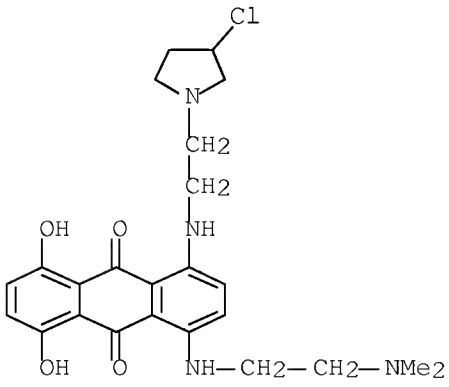
PAGE 1-A



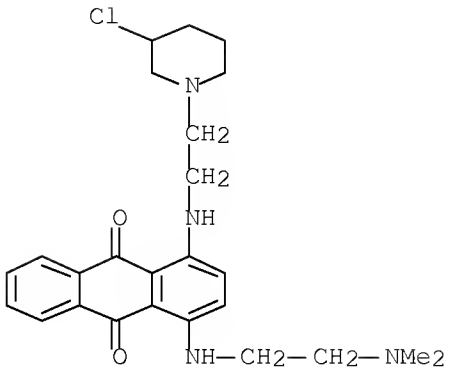
PAGE 2-A



RN 857637-39-9 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(3-chloro-1-pyrrolidinyl)ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



RN 857637-47-9 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(3-chloro-1-piperidinyl)ethyl]amino]-4-[[2-(dimethylamino)ethyl]amino]- (CA INDEX NAME)



RN 857637-48-0 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis[[2-[3-(chloromethyl)-1-piperidinyl]ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)

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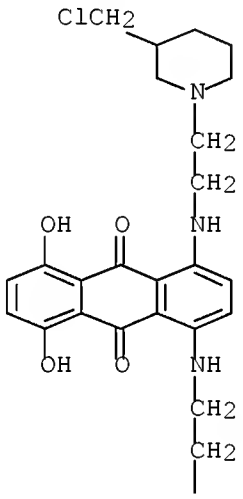
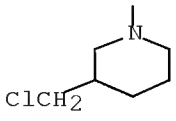


PAGE 2-A



RN 857637-49-1 HCAPLUS
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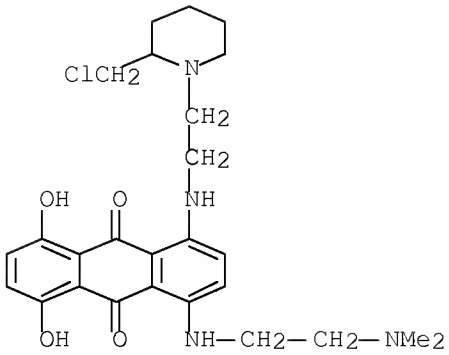

RN 857637-50-4 HCAPLUS
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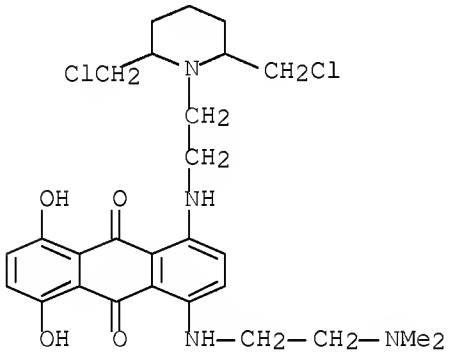
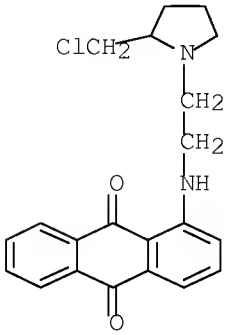
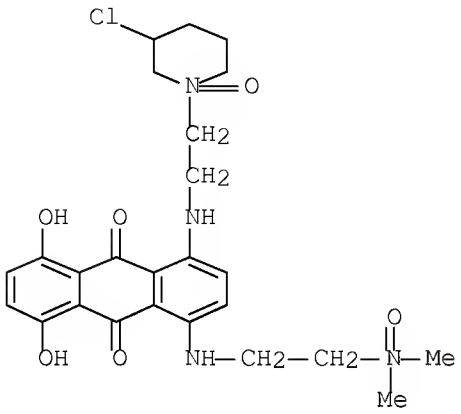


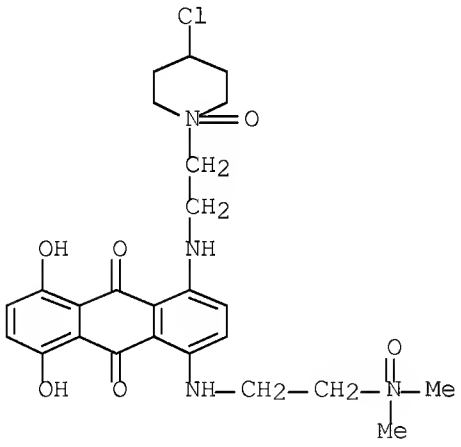
RN 857637-52-6 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[2-(chloromethyl)-1-pyrrolidinyl]ethyl]amino]- (CA INDEX NAME)



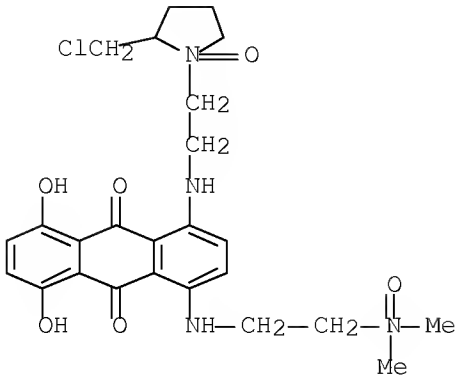
RN 857637-54-8 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(3-chloro-1-oxido-1-piperidinyl)ethyl]amino]-4-[[2-(dimethyloxidoamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



RN 857637-55-9 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(4-chloro-1-oxido-1-piperidinyl)ethyl]amino]-4-[[2-(dimethyloxidoamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



RN 857637-56-0 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-[2-(chloromethyl)-1-oxido-1-pyrrolidinyl]ethyl]amino]-4-[[2-(dimethyloxidoamino)ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)



RN 857637-57-1 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis[[2-[2-(chloromethyl)-1-oxido-1-piperidinyl]ethyl]amino]-5,8-dihydroxy- (CA INDEX NAME)

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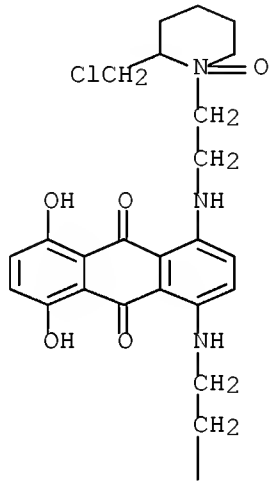

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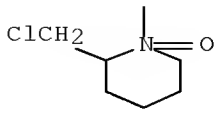
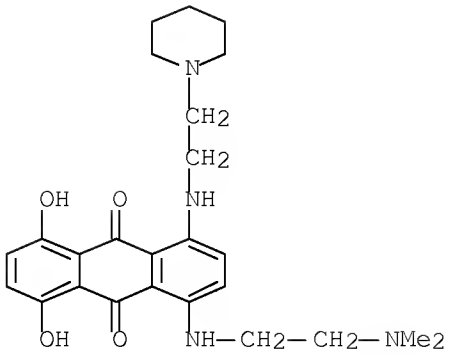
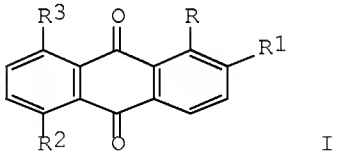


RN 857637-58-2 HCAPLUS
CN 9,10-Anthracenedione, 1-[[2-(dimethylamino)ethyl]amino]-5,8-dihydroxy-4-[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:594227 HCAPLUS Full-text
DOCUMENT NUMBER: 111:194227
ORIGINAL REFERENCE NO.: 111:32275a,32278a
TITLE: Synthesis of aminoanthraquinone derivatives and their in vitro evaluation as potential anti-cancer drugs
AUTHOR(S): Katzhendler, Jehoshua; Gean, Keria Fiorella; Bar-Ad, Gidon; Tashma, Zeev; Ben-Shoshan, Raphael; Ringel, Israel; Bachrach, Uriel; Ramu, Avner
CORPORATE SOURCE: Sch. Pharm., Hebrew Univ., Jerusalem, Israel
SOURCE: European Journal of Medicinal Chemistry (1989), 24(1), 23-30
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:194227
ED Entered STN: 25 Nov 1989
GI



I

AB Anthraquinones, e.g., I [R = NH(CH2)nNR42, R1 = R2 = R3 = H, R4 = H, Me, (CH2)mNH2; CH2CH2OH; R = R2 = R3 = H, R1 = NH(CH2)nR42; R = R2 = NH(CH2)nR42, R1 = R3 = H; R = R3 = NH(CH2)nNR42, R1 = R2 = H; n = 2, 3, 4; m = 2, 3], which are monosubstituted by aminoalkylamino side chains at positions 1, 2 or disubstituted at positions 1, 5 or 1, 8, were prepared Their in vitro cytotoxic activity was evaluated using P388 murine leukemia cells and a subline of these cells resistant to doxorubicin. The results of the structure-activity relationship anal. indicated that monosubstitution in position 1 or 2 showed a decrease of the activity when compared to adriamycin.

Disubstitution in positions 1, 5 by N,N-dimethylethylenediamine side chain led to optimal activity, whereas the presence of cyclic dialkylamino substituents in the same positions resulted in a corresponding decrease in the antitumor activity. Disubstitution in positions 1,8 did not show any improvement in the cytotoxic activity.

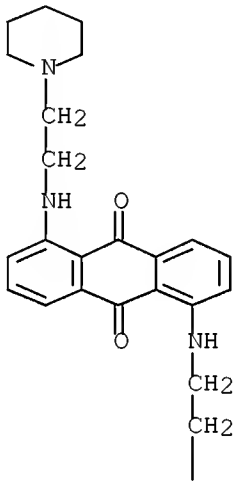
IT 123296-29-7P 123296-30-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and anticancer activity of)

RN 123296-29-7 HCAPLUS

CN 9,10-Anthracenedione, 1,5-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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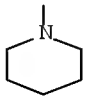
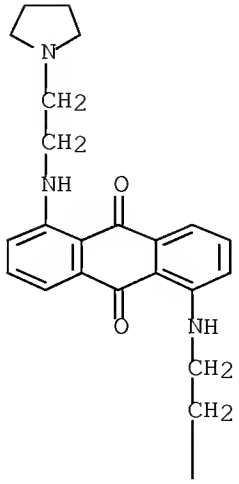


RN 123296-30-0 HCAPLUS

CN 9,10-Anthracenedione, 1,5-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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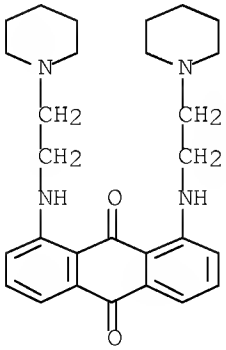
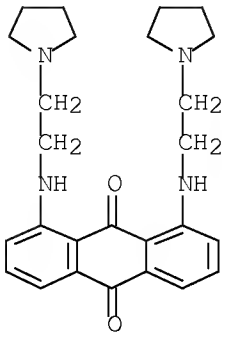
IT 123296-38-8P 123296-39-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and anticancer and bactericidal activities of)
RN 123296-38-8 HCAPLUS
CN 9,10-Anthracenedione, 1,8-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)



RN 123296-39-9 HCAPLUS
CN 9,10-Anthracenedione, 1,8-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX

NAME)



L15 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:205 HCAPLUS Full-text
DOCUMENT NUMBER: 108:205
ORIGINAL REFERENCE NO.: 108:27a,30a
TITLE: Relationship of chemical structures of anthraquinones with their effects on the suppression of immune responses
AUTHOR(S): Wang, Bosco Shang; Murdock, K. C.; Lumanglas, Araceli L.; Damiani, Martin; Silva, Jillian; Ruszala-Mallon, Veronica M.; Durr, Frederick E.
CORPORATE SOURCE: Lederle Lab., Am. Cyanamid Co., Pearl River, NY, 10965, USA
SOURCE: International Journal of Immunopharmacology (1987), 9(6), 733-9
CODEN: IJIMDS; ISSN: 0192-0561
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Jan 1988
AB A series of 37 anthraquinones was evaluated for their ability to inhibit the induction of cytolytic T-lymphocytes in a mixed lymphocyte culture system, useful as a preliminary screen for immunosuppressive agents. These compds. were also tested for their ability to prevent the production of antibody in mice. It was demonstrated that 1,4-bis[(2-aminoethyl)amino]- 5,8-dihydroxy-9,10-anthracenedione dihydrochloride (AEAD) derived from mitoxantrone (MX) by removing hydroxyethyl groups from both side chains was extremely active in depressing immune responses in vitro and in vivo. Four addnl. anthraquinones related to AEAD were also identified to share similar suppressive activity. These compds. may warrant further consideration as candidates for the treatment of refractory autoimmune diseases and in organ transplantation.
IT 70476-69-6
RL: BIOL (Biological study)
(immunosuppression by, structure in relation to)
RN 70476-69-6 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

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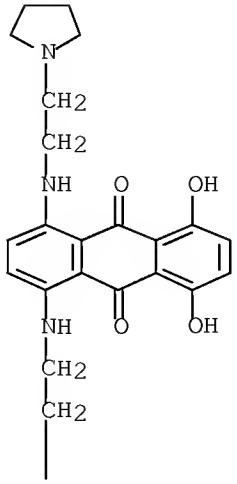

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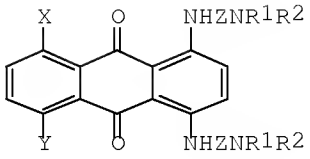
L15 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:4700 HCAPLUS Full-text
DOCUMENT NUMBER: 106:4700
ORIGINAL REFERENCE NO.: 106:875a,878a
TITLE: Pharmacologically active 1,4-diaminoanthraquinone derivatives
INVENTOR(S): Havlickova, Libuse; Kolonicky, Alois; Krepelka, Jiri; Obruba, Karel
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 11 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 231079	B1	19840917	CS 1982-5465	19820716
PRIORITY APPLN. INFO.:			CS 1982-5465	19820716

ED Entered STN: 11 Jan 1987
GI



I

AB Title compds. I (R1, R2 = H, alkyl, hydroxyalkyl, methylaminoalkyl, cycloalkyl; NR1R2 heterocyclyl; X, Y = H, OH, NHZNR1R2; Z = divalent hydrocarbyl) are prepared by condensation of the corresponding amines with the corresponding 1,4-dihydroxyanthraquinone derivs. (and their leuco forms). Thus, a mixture of 4.1 g quinizarin, 8.0 g leucoquinizarin, 15 mL water, and 12.4 g H2N(CH2)2NH(CH2)2OH was stirred under N for 1 h at room temperature, heated 2-6 h at 50-70° with thin-layer chromatog. control, and air-oxidized until disappearance of the leuco product form, to yield I (R1 = CH2CH2OH, R2 = X = Y = H, Z = CH2CH2).

IT 70476-69-6P 70945-59-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as drug)

RN 70476-69-6 HCAPLUS

CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

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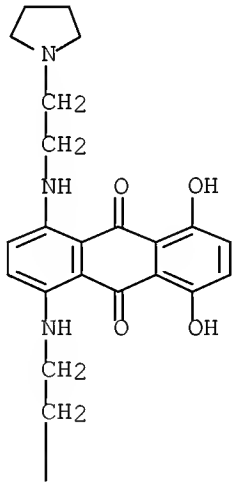

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RN 70945-59-4 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-piperidinyl)ethyl]amino]-
(CA INDEX NAME)

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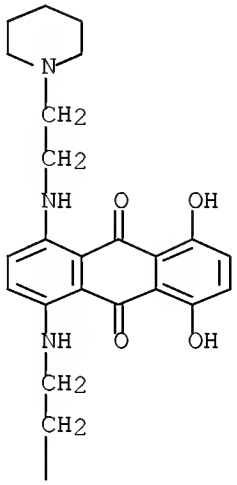

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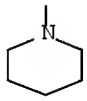
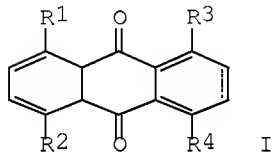


L15 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1986:82042 HCAPLUS Full-text
DOCUMENT NUMBER: 104:82042
ORIGINAL REFERENCE NO.: 104:12876h,12877a
TITLE: Inducing immunosuppression with 1,4-disubstituted anthraquinones
INVENTOR(S): Murdock, Keith Chadwick; Durr, Frederick Emil; Wang, Bosco Shang
PATENT ASSIGNEE(S): American Cyanamid Co. , USA
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 154117 A1 19850911 EP 1985-100307 19850114
EP 154117 B1 19891227
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE
AT 48942 T 19900115 AT 1985-100307 19850114
JP 60208939 A 19851021 JP 1985-34684 19850225
CA 1255300 A1 19890606 CA 1985-475025 19850225
AU 8539151 A 19850905 AU 1985-39151 19850226
AU 581878 B2 19890309
PRIORITY APPLN. INFO.: US 1984-583540 A 19840227
EP 1985-100307 A 19850114
OTHER SOURCE(S): MARPAT 104:82042
ED Entered STN: 22 Mar 1986
GI



I

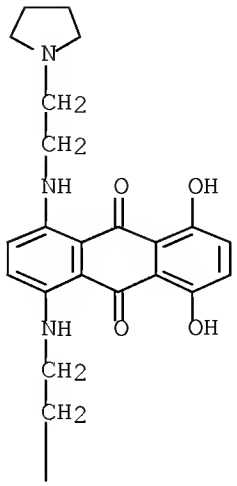
AB Immunosuppression is induced in mammals by the parenteral administration of 1,4-disubstituted anthraquinones. Compds. according to formula I (R1 and R2 = H or OH; R3 and R4 = substituted NHCH2CH2NH2, hydroxyalkylamines, substituted oxazoles, etc.) and their salts are prepared and their immunosuppressive activities examined Thus, 1,4-bis[(2-aminoethyl)amino]- 5,8-dihydroxyanthraquinone and BzH were heated under reflux for 4 h, filtered, and allowed to stand at room temperature for 13 days. The resulting compound (I; R1 and R2 = OH, R3 and R4 = NHCH2CH2N:CHPh) at 10-6 μg/mL induced ≥50% immunosuppression.

IT 70476-69-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as immunosuppressant)

RN 70476-69-6 HCAPLUS

CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A

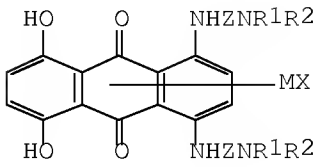


PAGE 2-A

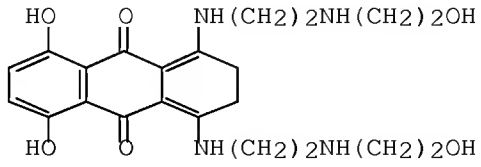
L15 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1982:122462 HCAPLUS Full-text
DOCUMENT NUMBER: 96:122462
ORIGINAL REFERENCE NO.: 96:20093a,20096a
TITLE: Metal chelates of 1,4-bis(substituted-amino)-5,8-dihydroxyanthraquinones
INVENTOR(S): Lang, Stanley Alber, Jr.; Murdock, Keith Chadwick
PATENT ASSIGNEE(S): American Cyanamid Co. , USA
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 37486	A2	19811014	EP 1981-101982	19810317
EP 37486	A3	19811021		
EP 37486	B1	19840125		
R: AT, BE, CH, DE, FR, GB, IT, NL, SE				
US 4296030	A	19811020	US 1980-138620	19800409
AT 5960	T	19840215	AT 1981-101982	19810317
JP 56156289	A	19811202	JP 1981-51898	19810408
JP 02055438	B	19901127		
PRIORITY APPLN. INFO.:			US 1980-138620 A	19800409

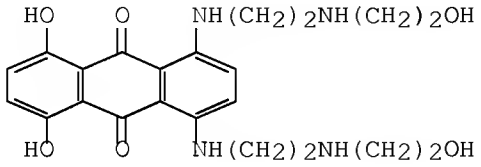
EP 1981-101982 A 19810317
OTHER SOURCE(S): MARPAT 96:122462
ED Entered STN: 12 May 1984
GI



I



II



III

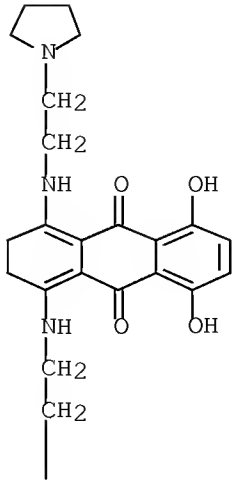
AB The title chelates I [Z = (CH2)n (n = 2-4), Me or Et-substituted ethylene, Me-substituted trimethylene; R1, R2 independently = H, C1-6 (hydroxy)alkyl, C3-6 dihydroxyalkyl, CHO, C2-4 alkanoyl, F3CCO, (CH2)nCN, (CH2)nOR (R = C1-4 alkyl), (CH2)nNR3R4 (R3, R4 independently = H, C1-4 alkyl, C2-4 hydroxyalkyl; NR3R4 = (thio)morpholino, (4-methyl)piperazino, C2-6 polymethyleneimino; M = Pt, Cu, Fe, Zr, Co, Cr, Zn; X = Cl, SO4, NO3] and their pharmacol. acceptable acid addition salts, useful for inhibiting the growth of transplanted mouse tumors, were prepared H2NCH2CH2NHCH2CH2OH in (Me2NCH2)2 was deaerated with bubbling N2 15 min and heated with leuco-1,4,5,8-tetrahydroxyanthraquinone 5 h at 50-52° to give leuco base II. This in MeOCH2CH2OH was treated with 8 N HCl in EtOH, then oxidized with chloranil to give anthraquinone salt III-2HCl which reacted with KOH and Pt chloride in MeOH to give III dichloride bis(Pt chloride chelate) (IV). The survival median for mice inoculated with lymphocytic leukemia P388 was 10 days with no treatment, 30 days for mice treated on days 1, 5 and 9 with 25 mg/kg IV, and 21 days for those similarly treated with 60 mg/kg 5-fluorouracil.

IT 70476-68-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of)

RN 70476-68-5 HCAPLUS

CN 9,10-Anthracenedione, 2,3-dihydro-5,8-dihydroxy-1,4-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

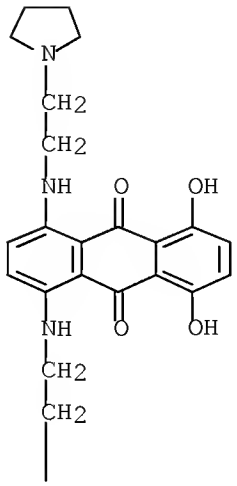
PAGE 1-A



PAGE 2-A

IT 70476-69-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 70476-69-6 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



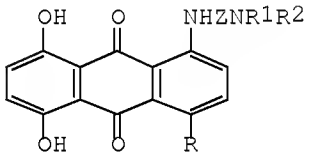
PAGE 2-A

L15 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:156626 HCAPLUS Full-text
DOCUMENT NUMBER: 94:156626
ORIGINAL REFERENCE NO.: 94:25597a,25600a
TITLE: 1-(aminoalkylamino)-5,8-dihydroxyanthraquinone derivatives
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 55160751	A	19801213	JP 1980-67957	19800523
JP 63061937	B	19881130		
US 4275009	A	19810623	US 1979-43271	19790529
CA 1148541	A1	19830621	CA 1980-347960	19800319
ZA 8001675	A	19810325	ZA 1980-1675	19800321
IL 59686	A	19831230	IL 1980-59686	19800321
AU 8056762	A	19801204	AU 1980-56762	19800324
AU 536826	B2	19840524		
FI 8001304	A	19801130	FI 1980-1304	19800423
ES 491876	A1	19810401	ES 1980-491876	19800527

DK 8002304	A	19801130	DK 1980-2304		19800528
NO 8001588	A	19801201	NO 1980-1588		19800528
NO 147643	B	19830207			
NO 147643	C	19830518			
DD 152334	A5	19811125	DD 1980-221420		19800528
HU 22706	A2	19820628	HU 1980-1342		19800528
HU 180355	B	19830228			
EP 21622	A1	19810107	EP 1980-301790		19800529
EP 21622	B1	19821020			
R: AT, BE, CH, DE, FR, GB, IT, NL, SE					
AT 1672	T	19821115	AT 1980-301790		19800529
PRIORITY APPLN. INFO.:			US 1979-43271	A	19790529
			EP 1980-301790	A	19800529

OTHER SOURCE(S): CASREACT 94:156626; MARPAT 94:156626
ED Entered STN: 12 May 1984
GI

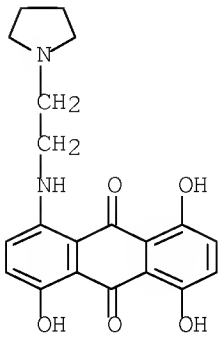


I

AB Anthraquinone derivs. (I; R = OH, alkylamino; R1, R2 = H, C1-4 alkyl, hydroxyalkyl, etc., Z = alkylene), effective antileukemic agents at 12.5-100 mg/kg and antitumor agents at 1.2-25 mg/kg in mice, were prepared Thus, a mixture of 52.9 g Me2NCH2CH2NH2 and 54.8 g leuco-1,4,5,8-tetrahydroxyanthraquinone in Me2NCH2CH2NMe2 was heated 2 h at 49-51° under N and chromatographed to give 3.4 g I (R = OH, R1 = R2 = Me, Z = CH2CH2). Similarly 6 addnl. I were prepared

IT 77184-74-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antileukemic activity of)

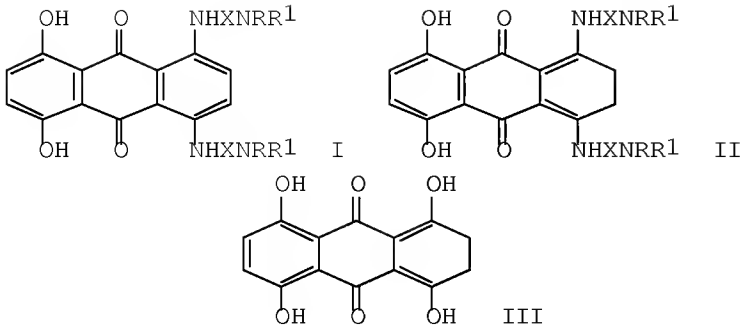
RN 77184-74-8 HCAPLUS
CN 9,10-Anthracenedione, 1,4,5-trihydroxy-8-[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)



L15 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:471396 HCAPLUS Full-text
DOCUMENT NUMBER: 93:71396
ORIGINAL REFERENCE NO.: 93:11601a,11604a
TITLE: 1,4-Bis(substituted amino)-5,8-dihydroxyanthraquinones and leuco bases thereof
INVENTOR(S): Durr, Frederick E.; Murdock, Keith C.
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: U.S., 18 pp. Cont.-in-part of U.S. Ser. No. 873,040 abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4197249	A	19800408	US 1978-923602	19780711
ZA 7804197	A	19790725	ZA 1978-4197	19780724
IL 64888	A	19860228	IL 1978-64888	19780726
BE 869688	A1	19790212	BE 1978-189842	19780811
CA 1140923	A1	19830208	CA 1978-309197	19780811
PL 122586	B1	19820831	PL 1978-209065	19780815
US 4278689	A	19810714	US 1979-63285	19790802
US 4526989	A	19850702	US 1979-87354	19791023
US 4456552	A	19840626	US 1981-239939	19810302
US 4430501	A	19840207	US 1981-244452	19811102
US 4540519	A	19850910	US 1984-598141	19840409
US 4614618	A	19860930	US 1985-757410	19850722
US 4820738	A	19890411	US 1986-823265	19860128
US 4888137	A	19891219	US 1987-42779	19870427
PRIORITY APPLN. INFO.:			US 1977-824872 A2	19770815
			US 1978-873040 A2	19780130
			US 1977-824822 A2	19770815
			US 1978-923602 A3	19780711
			IL 1978-55218 A	19780726
			US 1979-63285 A3	19790802
			US 1981-239939 A3	19810302
			US 1981-244452 A1	19811102
			US 1983-485143 A3	19830415
			US 1984-598141 A3	19840409

OTHER SOURCE(S): CASREACT 93:71396; MARPAT 93:71396
ED Entered STN: 12 May 1984
GI



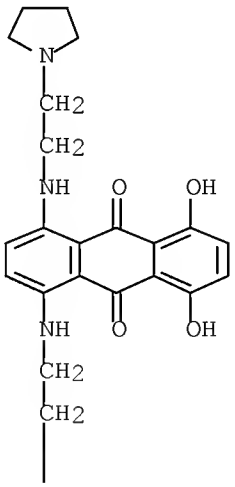
AB Anthraquinones I (X = (CH2)n, CHMeCH2, CHMeCHMe, CHEtCH2, CHMeCH2CH2, CH2CHMeCH2; n = 2-4; R,R1 = H, alkyl, hydroxyalkyl) and their leuco bases II were prepared Thus, III was treated with Me2NCH2CH2NH2 in Me2NCH2CH2NMe2 to give II (X = CH2CH2, R = H, R1 = CH2CH2NMe2, IV). Refluxing IV in nitrobenzene for 15 min gave I. In the lymphocytic leukemia P388 test using mice, IV had neoplasm inhibiting activity at 25 μg/kg i.p.

IT 70476-69-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and neoplasm inhibiting activity of)

RN 70476-69-6 HCAPLUS

CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

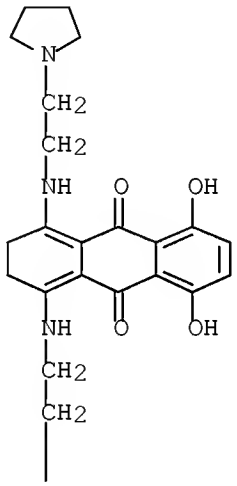
PAGE 1-A



PAGE 2-A

IT 70476-68-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, dehydrogenation and neoplasm inhibiting activity of)
RN 70476-68-5 HCAPLUS
CN 9,10-Anthracenedione, 2,3-dihydro-5,8-dihydroxy-1,4-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



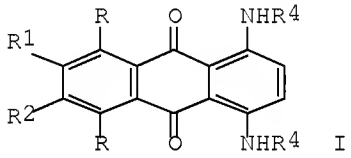
PAGE 2-A

L15 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:191505 HCAPLUS Full-text
DOCUMENT NUMBER: 92:191505
ORIGINAL REFERENCE NO.: 92:30924h,30925a
TITLE: Antineoplastic use of 1,4-bis(substituted aminoalkyl amino)anthraquinones
INVENTOR(S): Zee-Cheng, Robert K. Y.; Cheng, Chia-Chung
PATENT ASSIGNEE(S): United States Dept. of Health, Education, and Welfare, USA

SOURCE: U. S. Pat. Appl., 18 pp. Avail NTIS.
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 50100	A0	19791221	US 1979-50100	19790619
US 4310666	A	19820112		
US 895082	A0	19781208	US 1978-895082	19780410

PRIORITY APPLN. INFO.: US 1978-895082 19780410
ED Entered STN: 12 May 1984
GI



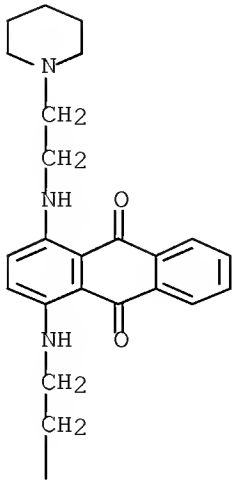
I

AB A method is described for treating animal neoplasms by the administration of the title compds. I (R, R1, R2, R3 = H, OH, halide, alkyl, substituted Ph, etc.; R4 = alkyl, alkylaminoalkyl, etc.). Thus, the antineoplastic activity of I against lymphocytic leukemia P388 was tested by implanting ascitic fluid in BDF1 mice and initiating treatment (i.p. administration daily for 9 days) 24 h after implant. Lymphoid leukemia L1210 and melanotic melanoma B16 were tested similarly. Structure-activity relations are presented.

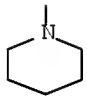
IT 65271-72-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm-inhibiting activity of)

RN 65271-72-9 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L15 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:174696 HCAPLUS Full-text
DOCUMENT NUMBER: 92:174696
ORIGINAL REFERENCE NO.: 92:28191a,28194a
TITLE: Antineoplastic use of 1,4-bis(substituted aminoalkylamino)anthraquinones
INVENTOR(S): Zee-Cheng, Robert K.-Y.; Cheng, Chia-Chung
PATENT ASSIGNEE(S): United States Dept. of Health, Education, and Welfare, USA
SOURCE: U. S. Pat. Appl., 18 pp. Avail. NTIS.
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 50330	A0	19791221	US 1979-50330	19790620

PRIORITY APPLN. INFO.: US 1979-50330 19790620
ED Entered STN: 12 May 1984
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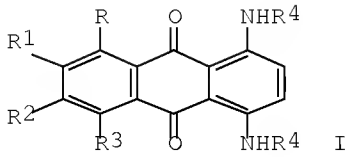


I

AB A method for treating animal neoplasms by administration to a host an antineoplastic amount of the title compds. I (R, R1, R2, R3 = H, OH, NH2, OMe, alkyl, etc.; R4 = alkyl, alkylaminoalkyl, substituted aminoaryl, etc.) is described. The antineoplastic activity of the various compds. was determined in in vitro testing with lymphoid leukemia L1210, lymphocytic leukemia P388, and melanotic melanoma B16 test systems. Thus, the activity against lymphocytic leukemia P338 was tested by implanting ascitic fluid in BDF1 mice. Treatment with I began 24 h after implant, and the increase of life span was determined Some structure-activity relations are presented.

IT 65271-72-9

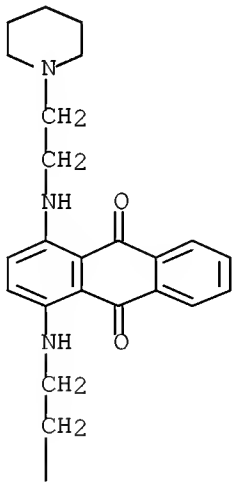
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antitumor activity of)

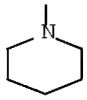
RN 65271-72-9 HCAPLUS

CN 9,10-Anthracenedione, 1,4-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

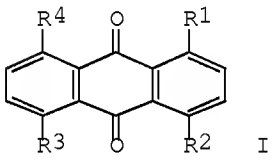
PAGE 1-A



PAGE 2-A



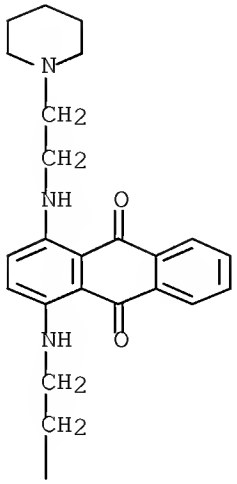
L15 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:116526 HCAPLUS Full-text
DOCUMENT NUMBER: 92:116526
ORIGINAL REFERENCE NO.: 92:18907a,18910a
TITLE: High-performance liquid chromatography of cancer chemotherapeutic agents: bis(substituted aminoalkylamino)anthraquinones
AUTHOR(S): Taylor, Richard F.; Gaudio, Linda A.
CORPORATE SOURCE: BioMol. Sci. Sect., Arthur D. Little, Inc., Cambridge, MA, 02140, USA
SOURCE: Journal of Chromatography (1980), 187(1), 212-17
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI



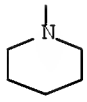
I

AB Twenty-five anthraquinones and bis(aminoalkylamino)anthraquinones [I, e.g., R1 = R2 = NH(CH2)2NH(CH2)2OH, R3 = R4 = H [64862-96-0]; R1 = R2 = (2-piperidinoethyl)amino, R3 = R4 = H [65271-72-9]; R1 = R3 = NH(CH2)3NMe2, R2 = R4 = H [70711-38-5]] were separated by high-performance liquid chromatog. The 2 most efficient systems used were: (1) μBondapak CN column, elution with a 15-min convex mobile phase gradient (curvature = 4) of 20-90% MeOH in 0.05M Na2HPO4-NaH2PO4, pH 8.0, and flow-rate of 2.0 mL/min; (2) μBondapak NH2 column, elution with a 15-min convex mobile phase gradient (curvature = 4) of 10-90% MeCN-MeOH (1:1) in 0.05M AcONH4-NH4OH, pH 8.0, and flow rate of 2.0 mL/min.
IT 65271-72-9
RL: ANT (Analyte); ANST (Analytical study)
(high-performance liquid chromatog. of)
RN 65271-72-9 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

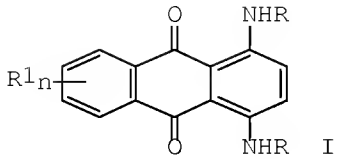
PAGE 1-A



PAGE 2-A



L15 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1979:501851 HCAPLUS Full-text
DOCUMENT NUMBER: 91:101851
ORIGINAL REFERENCE NO.: 91:16309a,16312a
TITLE: Antitumor agents. 1. 1,4-Bis[(aminoalkyl)amino]-9,10-anthracenediones
AUTHOR(S): Murdock, K. C.; Child, R. G.; Fabio, P. F.; Angier, Robert D.; Wallace, Roslyn E.; Durr, Frederick E.; Citarella, R. V.
CORPORATE SOURCE: Lederle Lab., American Cyanamid Co., Pearl River, NY, 10965, USA
SOURCE: Journal of Medicinal Chemistry (1979), 22(9), 1024-30
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 91:101851
ED Entered STN: 12 May 1984
GI



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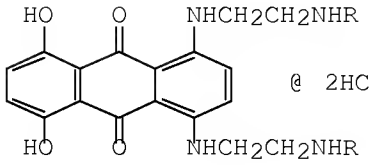


@ 2HCl

II, R=H
III, R=CH_2CH_2OH

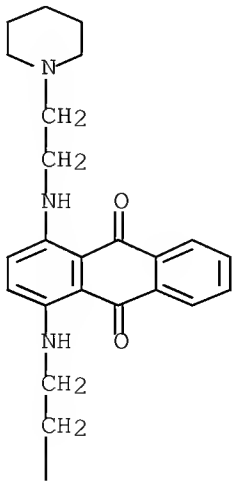
AB The condensation of alkylenediamines with quinizarin [81-64-1] or with 2,3-dihydro-1,4,5,8-tetrahydroxy-9,10-anthracenedione [70945-73-2], followed by oxidation, gave the title compds. I (R = H, CH2CH2NMe2, CH2CH2NHCH2CH2OH, etc.; R1 = H, Me, OH, etc.; n = 1 or 2). Some I and their 2,3-dihydro derivs. were active against both leukemias and solid tumors in mice. Against B-16 melanoma, II [70476-81-2] increased median life span (ILS)>433%. Against P-388 leukemia, III [70476-82-3] gave >500% ILS; its efficacy and therapeutic index equaled or surpassed those of Adriamycin, cyclophosphamide, daunorubicin, methotrexate, or 5-fluorouracil. III was as effective or more effective than Adriamycin against L-1210 leukemia, B16 melanoma, and colon tumor 26. Structure-activity relations are discussed.

IT 65271-72-9P 70476-69-6P 70945-59-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of)

RN 65271-72-9 HCAPLUS

CN 9,10-Anthracenedione, 1,4-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

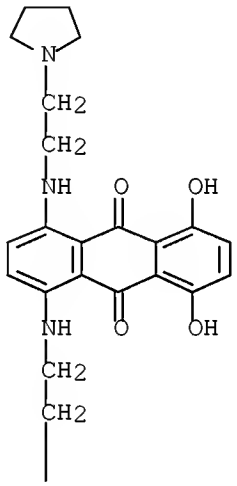
PAGE 1-A



PAGE 2-A

RN 70476-69-6 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

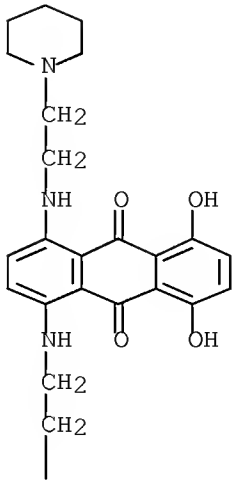
PAGE 1-A



PAGE 2-A

RN 70945-59-4 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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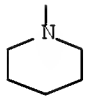

L15 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1979:456706 HCAPLUS Full-text
DOCUMENT NUMBER: 91:56706
ORIGINAL REFERENCE NO.: 91:9179a,9182a
TITLE: Substituted diaminoanthraquinones
INVENTOR(S): Murdock, Keith Chadwick; Durr, Frederick Emil; Child, Ralph Grassing
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Ger. Offen., 139 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2835661	A1	19790301	DE 1978-2835661	19780814
DE 2835661	C2	19910822		
US 4138415	A	19790206	US 1978-903292	19780505
ZA 7804197	A	19790725	ZA 1978-4197	19780724
CA 1099213	A1	19810414	CA 1978-308224	19780726
CA 1116522	A1	19820119	CA 1978-308128	19780726
IL 64888	A	19860228	IL 1978-64888	19780726
BE 869688	A1	19790212	BE 1978-189842	19780811
NL 7808475	A	19790219	NL 1978-8475	19780815

NL 188981	B	19920701			
NL 188981	C	19921201			
JP 54063064	A	19790521	JP 1978-99448		19780815
JP 01052365	B	19891108			
PL 122586	B1	19820831	PL 1978-209065		19780815
US 4418078	A	19831129	US 1979-69672		19790827
US 4540583	A	19850910	US 1980-214147		19801208
PRIORITY APPLN. INFO.:			US 1977-824872	A	19770815
			US 1978-873040	A	19780130
			US 1978-873041	A	19780130
			US 1978-873174	A	19780130
			US 1978-903292	A	19780505
			IL 1978-55218	A	19780726
			US 1978-965114	A1	19781130
			US 1979-63290	A2	19790802

OTHER SOURCE(S): CASREACT 91:56706; MARPAT 91:56706
ED Entered STN: 12 May 1984
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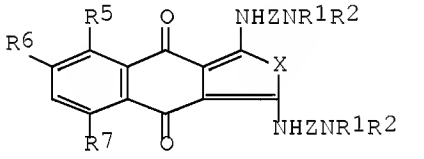

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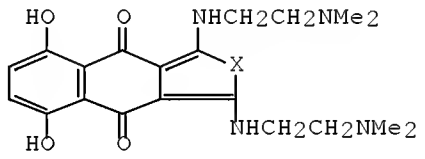


II

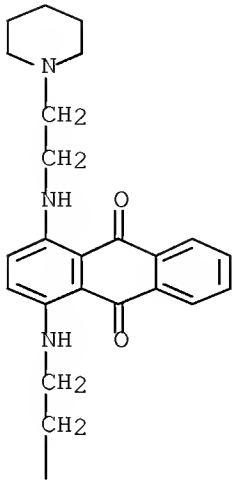
AB Sixty-three anthraquinones I [R1, R2 = H, C1-4 alkyl, C2-4 hydroxyalkyl, C3-6 dihydroxyalkyl, CHO, C2-4 alkanoyl, CF3CO, (CH2)mCN (m = 2-4), (CH2)mOR (R = C1-4 alkyl), (CH2)mNR3R4 (R3, R4 = H, C1-4 alkyl, C2-4 hydroxyalkyl), NR1R2, NR3R4 = morpholino, thiomorpholino, piperazino, 4-Me 1-piperazinyl, or (CH2)2-6; R5, R6 = H, OH; R7 = H, OH, NHCH2CH2NR8R9 (R8, R9 = Me, Et, HOCH2CH2; X = CH:CH, CH2CH2; Z = (CH2)m (m = 2-4), CHMeCH2, CH2CHMe, CHMeCHMe, CHEtCH2, CH2CHEt, CHMeCH2CH2, CH2CHMeCH2, CH2CH2CHMe], useful as inhibitors for tumors (extensive data tabulated), were prepared Thus, stirring Me2NCH2CH2NH2, (Me2NCH2)2, and leuco-1,4,5,8- tetrahydroxyanthraquinone under N2 2 h at 49-51° gave leucoanthraquinone II (X = CH2CH2), which on refluxing 15 min in PhNO2 gave II (X = CH:CH).

IT 65271-72-9P 70476-69-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of)

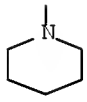
RN 65271-72-9 HCAPLUS

CN 9,10-Anthracenedione, 1,4-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A

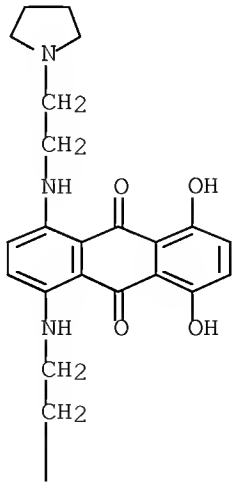


PAGE 2-A



RN 70476-69-6 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

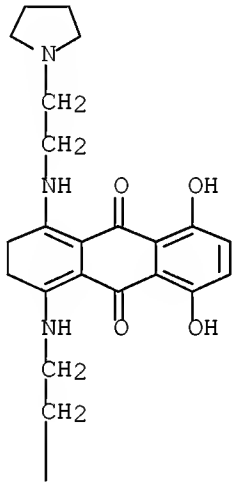
PAGE 1-A



PAGE 2-A

IT 70476-68-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, aromatization of, and antitumor activity of)
RN 70476-68-5 HCAPLUS
CN 9,10-Anthracenedione, 2,3-dihydro-5,8-dihydroxy-1,4-bis[[2-(1-pyrrolidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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L15 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1979:449685 HCAPLUS Full-text
DOCUMENT NUMBER: 91:49685

ORIGINAL REFERENCE NO.: 91:7951a
TITLE: Anti-neoplastic use of 1,4-bis-(substituted aminoalkylamino)-anthraquinones
INVENTOR(S): Zee-Cheng, R. K.; et al.
PATENT ASSIGNEE(S): USA
SOURCE: U. S. Pat. Appl., 18 pp. Avail NTIS.
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 895082	A0	19781208	US 1978-895082	19780410
CA 1143726	A1	19830329	CA 1979-324687	19790330
AU 7945744	A	19791018	AU 1979-45744	19790403
US 50100	A0	19791221	US 1979-50100	19790619
US 4310666	A	19820112		

PRIORITY APPLN. INFO.: US 1978-895082 A 19780410
OTHER SOURCE(S): MARPAT 91:49685
ED Entered STN: 12 May 1984
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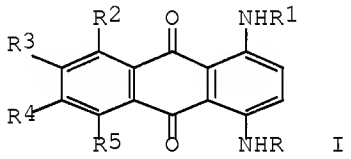


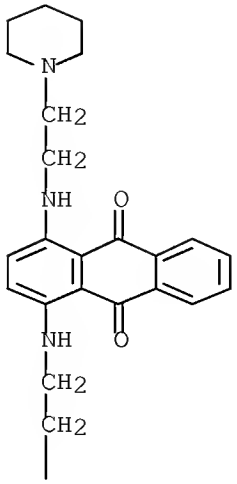
I

AB Various anthraquinone derivs. I were prepared and their neoplasm inhibiting activity was assessed in vivo. Most of I tested showed some neoplasm inhibiting activity. I; R = R1 = (CH2)2NH(CH2)2OH, R2 = R5 = OH, R3 = R4 = H [65271-80-9], I; R = R1 = (CH2)2NH(CH2)2OH, R2 = R3 = R4 = R5 = H [64862-96-0], and I; R = R1 = (CH2)2NH2, R2 = R3 = R4 = R5 = H [19853-95-3] were particularly active. Structural requirements for the antitumor activities of these agents are discussed.

IT 65271-72-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(neoplasm inhibiting activity of)

RN 65271-72-9 HCAPLUS
CN 9,10-Anthracenedione, 1,4-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

PAGE 1-A



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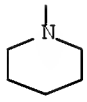

L15 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1979:432660 HCAPLUS Full-text
DOCUMENT NUMBER: 91:32660
ORIGINAL REFERENCE NO.: 91:5213a,5216a
TITLE: Experimental antitumor activity of aminoanthraquinones
AUTHOR(S): Johnson, Randall K.; Zee-Cheng, Robert K. Y.; Lee, William W.; Acton, Edward M.; Henry, David W.; Cheng, C. C.
CORPORATE SOURCE: Life Sci. Div., Arthur D. Little, Inc., Cambridge, MA, 02140, USA
SOURCE: Cancer Treatment Reports (1979), 63(3), 425-39
CODEN: CTRRDO; ISSN: 0361-5960
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
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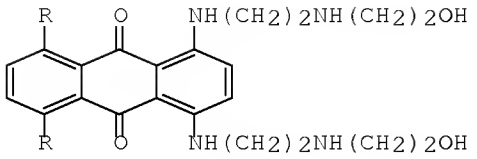


I, R=H
II, R=OH

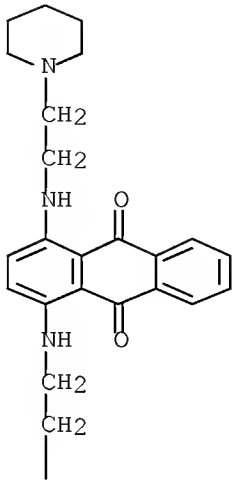
AB The activity of a number of substituted alkylaminoanthraquinones was compared in transplanted murine tumor systems including P388 and L1210 leukemias, B16 melanoma, and colon carcinoma 26. Structure-activity relations among this class of compds. are discussed. Several derivs. had very high antitumor activity in several tumor systems. Two of the most active derivs., 1,4-bis{2-[(2-hydroxyethyl)amino]ethylamino}-9,10-anthracenedione (I) [64862-96-0] and 1,4-dihydroxy-5,8-bis{2-[(2- hydroxyethyl)amino]ethylamino}-9,10-anthracenedione (II) [65271-80-9], which had curative activity in the above-mentioned tumors, were compared in considerable detail. II showed distinct advantages over I in several tumor systems and was 10-fold more potent with respect to ED range. This last difference is important for 2 reasons. First, these aminoanthraquinones are strong and persistent blue dyes and the administration of lower doses would minimize a potential cosmetic drawback of these compds. Second and most important, i.v. administration of dose levels of I which are within the therapeutic dose range on intermittent dose schedules produced convulsions and immediate death. I.v. administration of II also caused acute toxicity, but, because of its increase potency relative to antitumor activity and delayed toxicity, this acute toxicity was apparent only at doses well above the therapeutic dose range. All of the aminoanthraquinones evaluated, regardless of their activity as antitumor agents in vivo, proved to be potent inhibitors of DNA and RNA synthesis in vitro and bound strongly to DNA as evidenced by ΔTm values (ΔTm = upward shift in DNA melting temperature). Thus, the strong antitumor activity of aminoanthraquinones would appear to be due to some mechanism other than, or in addition to, DNA binding and inhibition of nucleic acid synthesis.

IT 65271-72-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of)

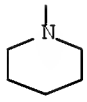
RN 65271-72-9 HCAPLUS

CN 9,10-Anthracenedione, 1,4-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

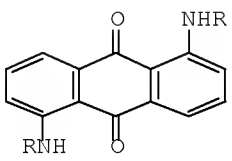
PAGE 1-A



PAGE 2-A



L15 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1979:162093 HCAPLUS Full-text
DOCUMENT NUMBER: 90:162093
ORIGINAL REFERENCE NO.: 90:25627a,25630a
TITLE: Antiviral and interferon-inducing properties of 1,5-diaminoanthraquinones
AUTHOR(S): Stringfellow, D. A.; Weed, S. D.; Underwood, G. E.
CORPORATE SOURCE: Exp. Biol. Res., Upjohn Co., Kalamazoo, MI, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1979), 15(1), 111-18
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI



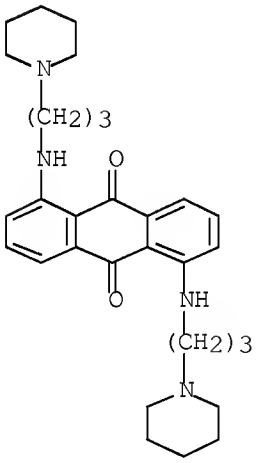
I

AB A series of anthraquinones with amino substituents at the 1,5 positions were found to induce interferon in mice. A prototype compound, I; R = 3-morpholinopropyl (II) [64686-26-6], was an effective antiviral agent when administered either orally or parenterally. Peak interferon titers were found 12 to 24 h after drug treatment. The min. oral dose of II required to induce serum interferon or to protect mice against a lethal virus infection was 62 mg/kg. Mice tolerated an oral dose of at least 30 times this min. ED. A single dose of II given up to 6 days prior to infection had significant protective activity. Biol. properties of II were compared with those of 3 other 1,5- diaminoanthraquinones, which also induced interferon and demonstrated antiviral activity in mice. The most active compound was I; R = Et2NCH2CH2 [1614-59-1] which protected mice against virus infection at a dose as low as 8 mg/kg (< 1/60 its maximum tolerated dose). Mice developed hyporeactivity to interferon induction if the same inducer was injected daily, although by alternating between different inducers the loss of interferon responsiveness could be avoided.

IT 1928-09-2
RL: BIOL (Biological study)
(interferon induction by, antiviral activity in relation to)

RN 1928-09-2 HCAPLUS

CN 9,10-Anthracenedione, 1,5-bis[[3-(1-piperidinyl)propyl]amino]- (CA INDEX NAME)



L15 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1978:83369 HCAPLUS Full-text

DOCUMENT NUMBER: 88:83369

ORIGINAL REFERENCE NO.: 88:13041a,13044a

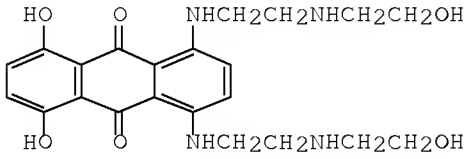
TITLE: Antineoplastic agents. Structure-activity relationship study of bis(substituted aminoalkylamino)anthraquinones

AUTHOR(S): Zee-Cheng, Robert K. Y.; Cheng, C. C.

CORPORATE SOURCE: Midwest Res. Inst., Kansas City, MO, USA

SOURCE: Journal of Medicinal Chemistry (1978), 21(3), 291-4
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI



I

AB Of 13 title compds. synthesized by condensation of various leucoquinizarins with appropriate amines, followed by air oxidation, several had activity against P-388 leukemia in mice, but only 1,4-dihydroxy-5,8- bis[[2-(hydroxyethyl)amino]ethyl]amino-9,10-anthracenedione (I) [65271-80-9] had potent inhibitory activity against both P-388 leukemia and B-16 melanoma systems. Both the position and the nature of the center N atom of the side chain were vital to the antineoplastic activity of these compds.

IT 65271-72-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antileukemic activity of)

RN 65271-72-9 HCAPLUS

CN 9,10-Anthracenedione, 1,4-bis[[2-(1-piperidinyl)ethyl]amino]- (CA INDEX NAME)

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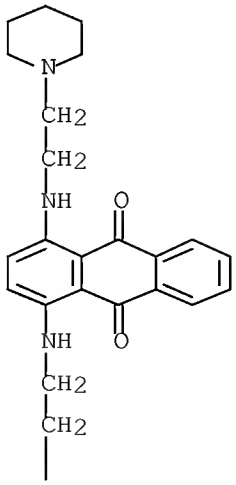
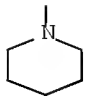
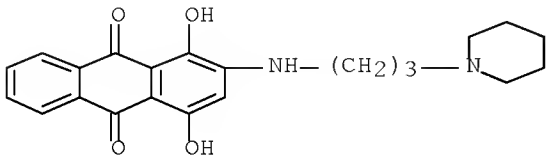




L15 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1975:520665 HCAPLUS Full-text
DOCUMENT NUMBER: 83:120665
ORIGINAL REFERENCE NO.: 83:18915a,18918a
TITLE: Colored nail polishes
INVENTOR(S): Kalopissis, Gregoire
PATENT ASSIGNEE(S): Oreal S. A., Fr.
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3849547	A	19741119	US 1971-112037	19710202
PRIORITY APPLN. INFO.:			US 1967-655741 A2	19670725
			US 1968-749315 A	19680801

ED Entered STN: 12 May 1984
GI For diagram(s), see printed CA Issue.
AB Nail polish vs lacquer consists of a solution of nitrocellulose [9004-70-0] film former 12-15, arenesulfonamide formaldehyde resin 6-13, plasticizer 5-8, coupler 1-15, diluent 12-32, soluble colored polymer 0.5-6 weight % (in which a dye is bonded to a polymer by an amide bond) and the remainder is solvent. Thus, a colored (red) polymer is prepared by treating Me vinyl ether-Bu maleate copolymer with the basic dye I. A transparent red polish comprises the red polymer 3, nitrocellulose 15, Santolite MHP [25035-71-6] 7.5, camphor 2.5, diBu phthalate 5, acetone 5, EtOAc 15, BuOAc 25, BuOH 4 and xylene 18 g.
IT 13269-98-2DP, 9,10-Anthracenedione, 1,4-dihydroxy-2-[[3-(1-piperidinyl)propyl]amino]-, reaction product with resins
RL: PREP (Preparation)
(preparation of, for nail polish)
RN 13269-98-2 HCAPLUS
CN 9,10-Anthracenedione, 1,4-dihydroxy-2-[[3-(1-piperidinyl)propyl]amino]- (CA INDEX NAME)



L15 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1974:451128 HCAPLUS Full-text

DOCUMENT NUMBER: 81:51128
ORIGINAL REFERENCE NO.: 81:8175a,8178a
TITLE: Anthraquinone dyes
INVENTOR(S): Kalopissis, Gregoire; Bertrand, Jacques; Bugaut, Andree
PATENT ASSIGNEE(S): Oreal S. A.
SOURCE: Ger., 4 pp.
CODEN: GWXXAW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1794332	B2	19740228	DE 1967-1794332	19640104
DE 1794332	C3	19750130		
DE 1794384	A1	19740502	DE 1967-1794384	19631029
DE 1794385	A1	19740502	DE 1967-1794385	19631029
US 3467483	A	19690916	US 1967-639915	19670519
US 3442895	A	19690506	US 1967-677068	19671023
US 3528972	A	19700915	US 1968-761297	19680920
NL 7000658	A	19700422	NL 1970-658	19700116
NL 7000660	A	19700422	NL 1970-660	19700116

PRIORITY APPLN. INFO.: FR 1963-920795 A 19630108
FR 1962-913810 A 19621029
FR 1963-930212 A 19630429
FR 1963-938822 A 19630620
US 1963-319635 A 19631024

ED Entered STN: 12 May 1984

AB Anthraquinone dye I(X = O, n = 2)(II) [1938-87-0] and anthraquinone dye I(X = CH2, n = 3) [1938-86-9] were prepared and dyed hair violet to gray shades. Thus, a mixture of quinizarin and N-(2- aminoethyl)morpholine was heated in EtOH to give 1-hydroxy-4-[(2- morpholinoethyl)amino]anthraquinone which was treated with Me2SO4 to give II, violet on gray hair. The other I was similarly prepared

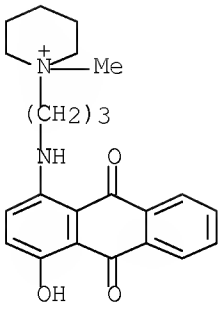
IT 1938-86-9P 2278-49-1P
RL: IMF (Industrial manufacture); PREP (Preparation)
(preparation of)

RN 1938-86-9 HCAPLUS

CN Piperidinium, 1-[3-[(9,10-dihydro-4-hydroxy-9,10-dioxo-1-anthracenyl)amino]propyl]-1-methyl-, methyl sulfate (salt) (9CI) (CA INDEX NAME)

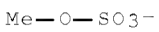
CM 1

CRN 47569-29-9
CMF C23 H27 N2 O3

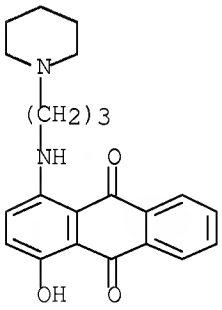


CM 2

CRN 21228-90-0
CMF C H3 O4 S



RN 2278-49-1 HCAPLUS
CN 9,10-Anthracenedione, 1-hydroxy-4-[[3-(1-piperidinyl)propyl]amino]- (CA INDEX NAME)



L15 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1972:568505 HCAPLUS Full-text
DOCUMENT NUMBER: 77:168505
ORIGINAL REFERENCE NO.: 77:27641a,27644a
TITLE: Hair dye
INVENTOR(S): Kalopissis, Gregoire; Bertrand, Jacques; Bugaut, Andree
PATENT ASSIGNEE(S): Oreal S. A.
SOURCE: Ger., 5 pp.
CODEN: GWXXAW
DOCUMENT TYPE: Patent
LANGUAGE: German

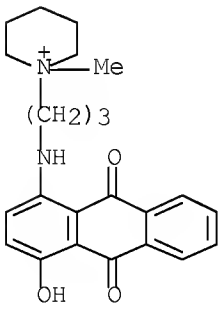
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1492066	C3	19730315	DE 1964-O9873	19640104
DE 1794384	A1	19740502	DE 1967-1794384	19631029
DE 1794385	A1	19740502	DE 1967-1794385	19631029
US 3467483	A	19690916	US 1967-639915	19670519
US 3442895	A	19690506	US 1967-677068	19671023
US 3528972	A	19700915	US 1968-761297	19680920
NL 7000658	A	19700422	NL 1970-658	19700116
NL 7000660	A	19700422	NL 1970-660	19700116
PRIORITY APPLN. INFO.:			FR 1963-920795 A	19630108
			FR 1962-913810 A	19621029
			FR 1963-930212 A	19630429
			FR 1963-938822 A	19630620
			US 1963-319635 A	19631024

ED Entered STN: 12 May 1984
GI For diagram(s), see printed CA Issue.
AB Anthraquinone dyes such as I (Z = morpholino) are used to dye hair violet at room temperature in 5-20 min at a pH of 3-9. Also used are I (Z = N-methylmorpholino Me sulfate, piperidinomethyl, N-methylpiperidinomethyl Me sulfate).
IT 1938-86-9
RL: BIOL (Biological study)
(dyes, hair)
RN 1938-86-9 HCAPLUS
CN Piperidinium, 1-[3-[(9,10-dihydro-4-hydroxy-9,10-dioxo-1-anthracenyl)amino]propyl]-1-methyl-, methyl sulfate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 47569-29-9
CMF C23 H27 N2 O3

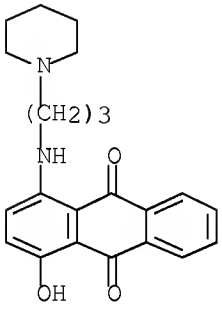


CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO3-

IT 2278-49-1P
RL: PREP (Preparation)
(preparation of)
RN 2278-49-1 HCAPLUS
CN 9,10-Anthracenedione, 1-hydroxy-4-[[3-(1-piperidinyl)propyl]amino]- (CA INDEX NAME)



L15 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1969:482718 HCAPLUS Full-text
DOCUMENT NUMBER: 71:82718
ORIGINAL REFERENCE NO.: 71:15405a,15408a
TITLE: Colored polymers useful in nail polishes or varnishes
INVENTOR(S): Kalopissis, Gregoire
PATENT ASSIGNEE(S): Oreal S. A.
SOURCE: Fr., 9 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1547495		19681129	FR 1967-115832	19670726
DE 1617721			DE	
GB 1193154			GB	
PRIORITY APPLN. INFO.:			LU	19660805
			LU	19670106

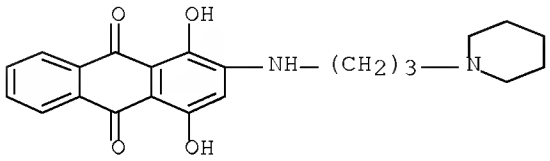
ED Entered STN: 12 May 1984
AB Transparent nail polishes with improved brilliancy were prepared Thus, a nail polish was prepared from nitrocellulose 15, Santolite MHP 7.5, camphor 2.5, di-Bu phthalate 5, colored polymer (I) 3, Me2CO 5, EtOAc 15, BuOAc 25, BuOH 4, and xylene 18 g. I was prepared by the amidation of methyl vinyl ether-Bu maleate copolymer (II) (Gantrez AN 3953) with 1-(3-aminopropylamino)anthraquinone. Other colored polymers were prepared by reaction of poly(itaconic anhydride), Me methacrylate-maleic anhydride copolymer, ethylene-maleic anhydride copolymer, or vinyl acetate-vinylpyrrolidone-N-allylchloroacetamide copolymer with basic dyes or by

copolymn. of 1-[(acryloylaminopropyl)-amino]anthraquinone with vinylpyrrolidone. The polish may contain TiO2.

IT 13269-98-2
RL: USES (Uses)
(polymers modified by, for manufacture of colored nail polishes)

RN 13269-98-2 HCAPLUS

CN 9,10-Anthracenedione, 1,4-dihydroxy-2-[[3-(1-piperidinyl)propyl]amino]- (CA INDEX NAME)



L15 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1966:3982 HCAPLUS Full-text
DOCUMENT NUMBER: 64:3982
ORIGINAL REFERENCE NO.: 64:671c-d
TITLE: Electrolytic production of sulfonic acids from condensed ring aromatic hydrocarbons
INVENTOR(S): Loveland, Junior W.
PATENT ASSIGNEE(S): Sun Oil Co.
SOURCE: 3 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3214356		19651026	US 1963-269191	19630329
PRIORITY APPLN. INFO.:			US	19630329

ED Entered STN: 22 Apr 2001

AB The title process involved the electrolysis of an aromatic hydrocarbon to produce a free radical which reacts in situ with SO3 to give a sulfonic acid anion. Thus, SO3 was bubbled into a saturated solution of anthracene (I) in 0.15M Et4NBr in dimethylformamide (DMF) containing 1% H2O at 150°F. in an electrolytic cell having a Hg cathode and a C anode while the solution was electrolyzed 8 hrs. at 2.1 v. This gave a solution of 9,10-dihydroanthracene-9,10-bis(sulfonic acid) (II), I, and Et4NBr in DMF. I and II were separated from the mixture by fractional distillation; II was separated from I by H2O extraction; the aqueous extract on cooling gave crystalline II.

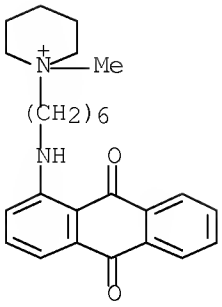
IT 7111-48-0P, Piperidinium compounds, 1-[6-(1-anthraquinonylamino)hexyl]-1-methyl-, methyl sulfate
RL: PREP (Preparation)
(preparation of)

RN 7111-48-0 HCAPLUS

CN Piperidinium, 1-[6-(1-anthraquinonylamino)hexyl]-1-methyl-, methyl sulfate (8CI) (CA INDEX NAME)

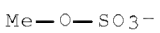
CM 1

CRN 47647-09-6
CMF C26 H33 N2 O2



CM 2

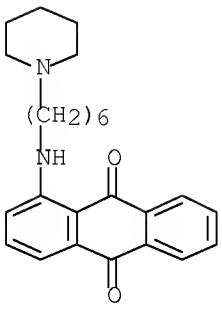
CRN 21228-90-0
CMF C H3 O4 S



L15 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1966:3981 HCAPLUS
DOCUMENT NUMBER: 64:3981
ORIGINAL REFERENCE NO.: 64:671c
TITLE: α-(ω-Dialkylaminopolymethylenamino)anthraquinones
INVENTOR(S): Russkikh, V. V.; Fokin, E. P.
PATENT ASSIGNEE(S): Institute of Organic Chemistry Siberian Dept., Academy of Sciences, U.S.S.R.
SOURCE From: Byul. Izobret. i Tovarnykh Znakov 1965(14), 63-4..
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SU 172940		19650707	SU	19640203

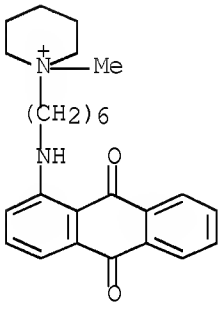
PRIORITY APPLN. INFO.: SU 19640203
ED Entered STN: 22 Apr 2001
AB N-(Anthraquinonyl-α)-ω-aminoaliphatic aldehydes are subjected to reductive amination with fatty secondary amines and formic acid.
IT 4662-23-1P, Anthraquinone, 1-[(6-piperidinohexyl)amino]-
7111-48-0P, Piperidinium, 1-[6-(1-anthraquinonylamino)hexyl]-1-methyl-, methyl sulfate
RL: PREP (Preparation)
(preparation of)
RN 4662-23-1 HCAPLUS
CN Anthraquinone, 1-[(6-piperidinohexyl)amino]- (7CI, 8CI) (CA INDEX NAME)



RN 7111-48-0 HCAPLUS
CN Piperidinium, 1-[6-(1-anthraquinonylamino)hexyl]-1-methyl-, methyl sulfate (8CI) (CA INDEX NAME)

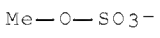
CM 1

CRN 47647-09-6
CMF C26 H33 N2 O2



CM 2

CRN 21228-90-0
CMF C H3 O4 S



L15 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1966:3980 HCAPLUS Full-text
DOCUMENT NUMBER: 64:3980
ORIGINAL REFERENCE NO.: 64:671a-c
TITLE: s-Octahydroanthracene
PATENT ASSIGNEE(S): Bergwerksverband G.m.b.H.

SOURCE: 6 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1409078		19650820	FR 1964-989311	19640925
BE 653277			BE	
GB 1007305			GB	
PRIORITY APPLN. INFO.:			DE	19631113

ED Entered STN: 22 Apr 2001

AB Partial hydrogenation of 40% strength anthracene at high temperature and pressure in the presence of a catalyst unaffected by S, gave a crude mixture, from which s-octahydroanthracene (I) of high quality was distilled The starting material was obtained by distilling coal-tar and then washing and centrifuging the 30% strength anthracene fraction. For example, a mixture of 100 parts by weight 40% strength anthracene and 1 part Co and Mo oxides was stirred in an autoclave at 350° and treated with H at 200 atmospheric until 500 1. (at normal temperature and pressure) had been absorbed. The crude product was fractionated through a column of approx. 80 theoretical plates to give 33 parts (80% yield) I (90% strength), b12 160-3°. The process is superior to previous ones in which high quality I is prepared by reduction of high quality anthracene, obtainable only by recrystn. of crude anthracene in pyridine bases. The crude partially hydrogenated mixture is separable by distillation, whereas separation of the mixture of aromatic starting materials by distillation is practically impossible.

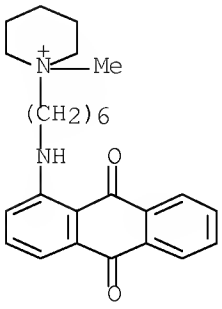
IT 7111-48-0P, Piperidinium, 1-[6-(1-anthraquinonylamino)hexyl]-1-methyl-, methyl sulfate
RL: PREP (Preparation)
(preparation of)

RN 7111-48-0 HCAPLUS

CN Piperidinium, 1-[6-(1-anthraquinonylamino)hexyl]-1-methyl-, methyl sulfate (8CI) (CA INDEX NAME)

CM 1

CRN 47647-09-6
CMF C26 H33 N2 O2



CM 2

CRN 21228-90-0
CMF C H3 O4 S

Me—O—SO3-

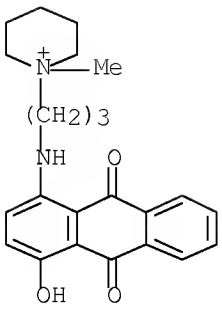
L15 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:463701 HCAPLUS Full-text
DOCUMENT NUMBER: 63:63701
ORIGINAL REFERENCE NO.: 63:11745c-e
TITLE: 1-[(ω -Dialkylaminoalkyl)amino] - 4 - hydroxyanthraquinones
INVENTOR(S): Kalopissis, Gregoire; Bertraud, Jacques; Bugaut, Andree
PATENT ASSIGNEE(S): L'Oreal
SOURCE: 13 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 642008		19640630	BE 1964-2008	19631231
FR 1391675			FR	
NL 302452			NL	
PRIORITY APPLN. INFO.:			FR	19630108

ED Entered STN: 22 Apr 2001
GI For diagram(s), see printed CA Issue.
AB Compds. of the general formula I and salts of the general formula II are prepared and can be used to dye hair. Thus, a solution of 0.2 mole quinizarin and 0.24 mole N-(β-aminoethyl)morpholine in 150 ml. iso-BuOH is refluxed 3 hrs. to give 1-[(β-morpholinoethyl)amino]-4- hydroxyanthraquinone, m. 164-5° (C6H6). Similarly prepared is I(n = 3, X = CH2), m. .apprx.105° (alc.). Also prepared are (m.p. given): II (n = 2, X = O) (III), 200-5° (decomposition); II (n = 3, X = CH2), 160-3° (decomposition). A solution (100 ml., pH 9) containing 5 g. III, 10 g. condensation product of C12-14 copra alc. + 10 moles ethylene oxide, and Na2CO3 in H2O is applied on gray hairs and, after 10-15 min. at room temperature, the hairs are rinsed and dried to give an intense violet color.
IT 1938-86-9P, Piperidinium, 1-[3-[(9,10-dihydro-4-hydroxy-9,10-dioxo-1-anthracenyl)amino]propyl]-1-methyl-, methyl sulfate (salt)
2278-49-1P, Anthraquinone, 1-hydroxy-4-[(3-piperidinopropyl)amino]-
RL: PREP (Preparation)
(preparation of)
RN 1938-86-9 HCAPLUS
CN Piperidinium, 1-[3-[(9,10-dihydro-4-hydroxy-9,10-dioxo-1-anthracenyl)amino]propyl]-1-methyl-, methyl sulfate (salt) (9CI) (CA INDEX NAME)

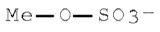
CM 1

CRN 47569-29-9
CMF C23 H27 N2 O3

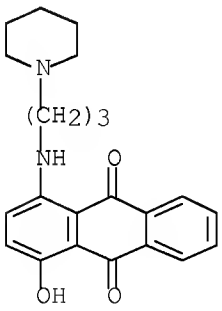


CM 2

CRN 21228-90-0
CMF C H3 O4 S



RN 2278-49-1 HCAPLUS
CN 9,10-Anthracenedione, 1-hydroxy-4-[[3-(1-piperidinyl)propyl]amino]- (CA INDEX NAME)



L15 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:410022 HCAPLUS Full-text
DOCUMENT NUMBER: 63:10022
ORIGINAL REFERENCE NO.: 63:1757a-e
TITLE: 1,5(or 1,8)-Diaminoanthraquinones
INVENTOR(S): Turner, Arthur G.; Sharp, Thomas M.
PATENT ASSIGNEE(S): Wellcome Foundation Ltd.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 985970		19650310	GB 1960-28209	19600815
PRIORITY APPLN. INFO.:			GB	19600815

ED Entered STN: 22 Apr 2001

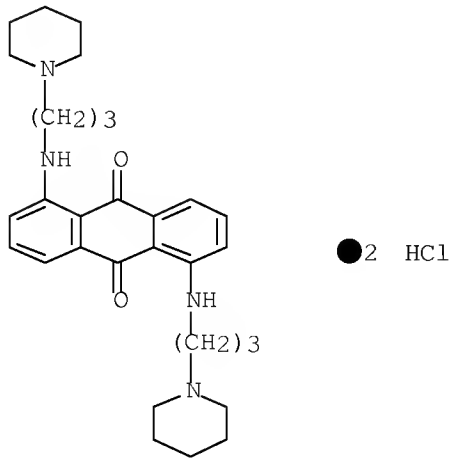
GI For diagram(s), see printed CA Issue.

AB Compds. of the general formulas I and II, where n = 2 to 10, NR1R2 is NMe2, NEt2, NMeEt, piperidino (III), 4-methyl-1-piperazinyl (IV), or hexamethylenimino (V) and Z = H or Me, and their acid addition salts were prepared by treating corresponding 1,5(or 1,8)-disubstituted anthraquinones with an ω-disubstituted amino alkylene amine. Thus, 30 g. 1,5-dichloroanthraquinone, 40 ml. 2-diethylaminoethylamine, 20 g. K2CO3, 1.2 g. Cu powder, 2.4 g. Cu(OAc)2.H2O, and 180 ml. amyl alc. was refluxed 20 hrs., steam distilled, the residue was acidified with dilute HCl, filtered, and the filtrate was made alkaline with NH4OH to give 1,5-bis(2-diethylaminoethylamino)anthraquinone, purple-brown, m. 163-5° (alc.); dihydrobromide, scarlet needles, m. 303°. Other anthraquinones were similarly prepared and are tabulated. 1,5-Bis(4-diethylamino-1-methylbutylamino) anthraquinone binoxalate, m. 177-9°, was also prepared Formula, n, NR1R2, Z, M.p., Salt, M.p.; I, 2, NMe2, H, 188-90°, 2HCl, 317° (decomposition); I, 3, NMe2, H, -, 2HCl, 287-9°; I, 3, NEt2, H, -, 2HCl, 285-7°; I, 4, NEt2, H, -, 2HCl, 238-240°; I, 5, NEt2, H, 115°, 2HCl, 235-6°; I, 3, III, H, 104-7°, 2HCl, 283-5°; I, 2, V, H, 175-7°, 2HCl, 327° (decomposition); I, 3, IV, H, -, 4HCl, 295°; I, 10, NEt2, H, -, 2HBr, 213-15°; I, 2, NEt2, Me, -, 2HCl, 260-5°; II, 2, NEt2, H, -, 2HCl, 263-5°; II, 3, NEt2, H, -, 2HCl, 282-4°; The products were active against infections of Hymenolepis nana and Oochoristica symmetrica in mice as compns. in capsules and cachets of the acid addition salts and an acceptable carrier.

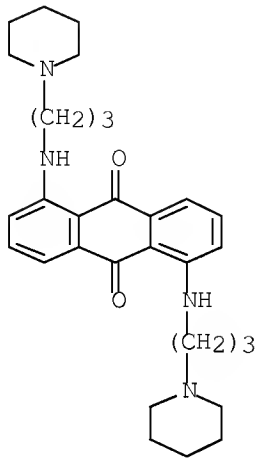
IT 1787-01-5P, Anthraquinone, 1,5-bis[(3-piperidinopropyl)amino]-, dihydrochloride 1928-09-2P, Anthraquinone, 1,5-bis[(3-piperidinopropyl)amino]-
RL: PREP (Preparation)
(preparation of)

RN 1787-01-5 HCAPLUS

CN Anthraquinone, 1,5-bis[(3-piperidinopropyl)amino]-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



RN 1928-09-2 HCAPLUS
CN 9,10-Anthracenedione, 1,5-bis[[3-(1-piperidinyl)propyl]amino]- (CA INDEX NAME)



L15 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:67011 HCAPLUS Full-text
DOCUMENT NUMBER: 62:67011
ORIGINAL REFERENCE NO.: 62:11947d-g
TITLE: Anthraquinone hair dyes
INVENTOR(S): Kalopissis, Gregoire; Bertrand, Jacques; Bugaut, Andree
PATENT ASSIGNEE(S): Oreal S.A.
SOURCE: 24 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 639298		19640429	BE	
NL 299891			NL	
PRIORITY APPLN. INFO.:			FR	19621029

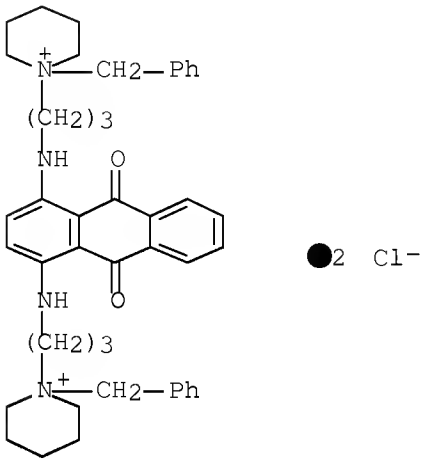
ED Entered STN: 22 Apr 2001
GI For diagram(s), see printed CA Issue.
AB Compds. of the general formula I, where m and n are 0-6, and Z and Z' are morpholino, piperidino, p-Me2NC6H4, or Me2N groups, and their quaternary salts, are hair dyes. Thus, a mixture of 0.06 mole quinizarin, 0.06 g.-atom Zn, and 0.2 mole N-(β-aminoethyl)morpholine in 100 ml. iso-BuOH was refluxed 3 hrs., the intermediate leuco derivative oxidized, the Zn filtered, the mixture evaporated to dryness, the residue dissolved in C6H6, the solution washed with 10 % aqueous Na2CO3, dried and evaporated to dryness, to give 90% I (m = n = 2, Z = Z' = morpholino, position of NH(CH2)nZ' = 4) (II), m. 157° (hexane), which dyed 95%-white hair blue green. II was refluxed in PhMe with Me2SO4 to give the double quaternary salt m. 240-5° (decompose) (MeOH), which dyed gray hair blue. Similarly, other I were prepared, where m = n and Z = Z' (m, Z, position of NH(CH2)nZ' group, m.p., quaternizing agent, m.p. salt, original hair color, and shade given): 2, morpholino, 5, 203° (dyed gray hair pink),

Me2SO4, 250° (decompose), gray, violet-pink; 6, morpholino, 4, 71° (heptane), Me2SO4, --, --, --; 2, morpholino, 8, 170-1° (hexane), Me2SO4, 200-1° (decompose) (alc.), gray, violet; 3, piperidino, 4, 123° (petr. ether-alc.), PhCH2Cl, 165-70° (decomposition), --, --; 0, p-Me2NC6H4, 4, 275° (PHCl), Me2SO4, 286-8° (decompose), 95%-white, orange; 0, p-Me2NC6H4, 5, 188° (CHCl3-C6H6), Me2SO4, --, 95%-white, orange red. Also prepared was 1-(p-dimethylaminoanilino)-4-(2- morpholinoethyl)aminoanthraquinone, m. 226° (dioxane), its bis(methosulfate) dyeing 95%-white hair blue green.

IT 3008-78-4
(Derived from data in the 7th Collective Formula Index (1962-1966))

RN 3008-78-4 HCAPLUS

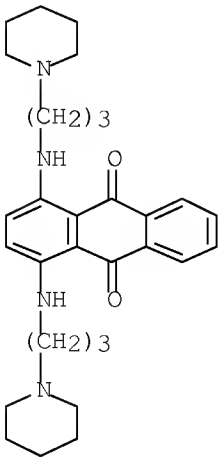
CN Piperidinium, 1,1'-[1,4-anthraquinonylenebis(iminotrimethylene)]bis[1-benzyl-, dichloride (8CI) (CA INDEX NAME)



IT 3008-79-5P, Anthraquinone, 1,4-bis[(3-piperidinopropyl)amino]-
RL: PREP (Preparation)
(preparation of)

RN 3008-79-5 HCAPLUS

CN Anthraquinone, 1,4-bis[(3-piperidinopropyl)amino]- (7CI, 8CI) (CA INDEX NAME)



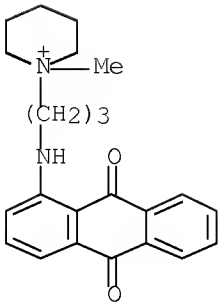
L15 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:52199 HCAPLUS Full-text
DOCUMENT NUMBER: 62:52199
ORIGINAL REFERENCE NO.: 62:9275e-h,9276a
TITLE: Vat dyes
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 10 pp.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 966497		19640812	GB 1962-20676	19620529
PRIORITY APPLN. INFO.:			CH	19610602

ED Entered STN: 22 Apr 2001
GI For diagram(s), see printed CA Issue.
AB The title compds. contain ≥1 allylmercapto or allyl sulfone group and are prepared by a variety of acylation or alkylation reactions. Thus, 2 parts 1,5-diaminoanthraquinone in 40 parts hot o-C6H4Cl2 is refluxed 0.5 h. with 3.56 parts 4-CH2:CHCH2SC6H4COCl (I) and the cooled mixture filtered to give II, m. 268-70°, yellow on cotton. I, pale yellow oil, b14 170°, is prepared from SOCl2 and 4-CH2: CHCH2SC6H4CO2H (III), m. 114°, obtained by treating 4-HSC6H4CO2H with CH2:CHCH2Cl in alc. KOH. Other dyes prepared are (reactants in order, color on cotton given): 1-aminoanthraquinone, 2-(4-allylsulfonylphenyl)benzothiazole-6-carboxylic acid chloride (IV), green-yellow; 1,4-diamino-2-acetylanthraquinone, IV, blue; 4-CH2:CHCH2SO2C6H4COCl (V), 4,4'-diamino-1,1'-dianthrimidecarbazole, olive-gray; aminoacedianthone, I, brown; 5,5'-diamino-1,1'- dianthrimidecarbazole, 3-CH2:CHCH2SC6H4COCl (VI), light brown; 1-benzamido-5-(4,6-dichloro-2-triazinylamino)anthraquinone (VII), CH2:CH-CH2SH, yellow; 1,4-diamino-2-anthraquinonyl-2',3'-anthraquinonothiazole, VI, blue; 4,10-dimercaptoanthanthrone, CH2: CHCH2Cl, violet; VII, 4-CH2:CHCH2SO2C6H4NH2 (VIII) (cf. Baker and Querry, CA 44, 7261d), yellow; 2-chloro-4,6-bis(1-anthraquinonylamino)-s-triazine, VIII, yellow; 2,5-bis(1,4-diamino-2-anthraquinonyl)-1,3,4-oxadiazole, V, dark violet-blue; IX, VIII, yellow; 1-amino-6- (allylmercapto)anthraquinone, BzCl, greenish yellow. IV, m. 225-6°, is prepared from SOCl2 and the corresponding acid, the latter, m. 284-5°, being obtained by treating V with 5,2-HO2C(H2N)C6H3SH.HCl in pyridine. III and H2O2 give 4-CH2:CHCH2SO2C6H4CO2H, m. 172-6°, acid chloride (V), m. 114-15°.
IT 2784-01-2P, Piperidinium, 1-[3-[(9,10-dihydro-9,10-dioxo-1-anthracenyl)amino]propyl]-1-methyl-, methyl sulfate 2784-02-3P, Anthraquinone, 1-[(3-piperidinopropyl)amino]-
RL: PREP (Preparation)
(preparation of)
RN 2784-01-2 HCAPLUS
CN Piperidinium, 1-[3-[(9,10-dihydro-9,10-dioxo-1-anthracenyl)amino]propyl]-1-methyl-, methyl sulfate (9CI) (CA INDEX NAME)

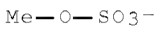
CM 1

CRN 47531-63-5
CMF C23 H27 N2 O2

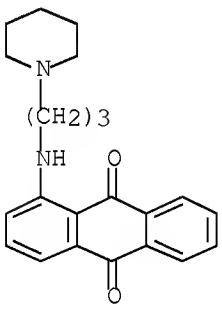


CM 2

CRN 21228-90-0
CMF C H3 O4 S



RN 2784-02-3 HCAPLUS
CN Anthraquinone, 1-[(3-piperidinopropyl)amino]- (7CI, 8CI) (CA INDEX NAME)



L15 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:3446 HCAPLUS Full-text
DOCUMENT NUMBER: 62:3446
ORIGINAL REFERENCE NO.: 62:665e-h,666a
TITLE: Synthesis, and use in hair preparations, of some quaternary dyes from anthraquinone
AUTHOR(S): Kalopissis, G.; Bugaut, A.; Bertrand, J.
CORPORATE SOURCE: Res. Labs., L'Oreal, Aulnay-sous-Bois, Fr.
SOURCE: Journal of the Society of Cosmetic Chemists (1964), 15(8), 411-20, discussion 420-2
CODEN: JSCCA5; ISSN: 0037-9832
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

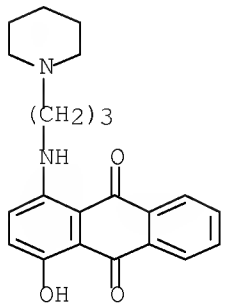
ED Entered STN: 22 Apr 2001

AB The preparation and behavior of new quaternary dyes derived from 2-aminoanthraquinone (I), 1-hydroxy-4-aminoanthraquinone (II), and 1-hydroxy-2,4-diaminoanthraquinone (III) are described. 2-Chloroanthraquinone (19.4 g.), 41.6 g. β-aminoethylmorpholine, and 60 ml. pyridine heated 7 hrs. at 135°, cooled, centrifuged to remove solids, concentrated in vacuo, extracted with 500 ml. M HCl, clarified, and adjusted to pH 7.5 gave a crude solid, which, when chromatographed over alumina (C6H6-n-C6H14) afforded 2-(β-morpholinoethyl)aminoanthraquino ne (IV), m. 190° (alc.), in 25% yield. V and Me2SO4 heated 30 min. at 110-15° in PhCl gave 91% 2-(β-methylmorpholinoethylamino)an thraquinone methosulfate (V). Similarly prepared were 2-(β- trimethylammonioethylamino)anthraquinone methosulfate (VI) and 2-(β-methyldiethylammonioethylamino)anthraquinone methosulfate (VII). A mixture of 165 g. I, 485 g. Et2NC2H4Cl, and 1600 ml. PhNO2 heated 2 hrs. at 180° gave a free base, m. 123°, in 73% yield, which with Me2SO4 in refluxing C6H6 afforded 93% VII. A mixture of 36 g. quinizarin (VII), 24.2 g. 4-(γ-aminopropyl)piperidine, and 225 ml. MePh was heated 7 hrs., 24 g. (CO2H)2 in Et2O added, the oxalate (61 g.) air dried, dissolved in H2O, adjusted to pH 8.5 with NaOH, and extracted with Et2O to give free base, m. 105° (C6H14), which with Me2SO4 in MePh at room temperature afforded 90% 1-hydroxy-4-(γ-methylpiperidinopropylamino)anthra quinone methosulfate (VIII). A mixture of 840 g. IV, 455 g. β-aminoethylmorpholine, 2500 ml. iso-BuOH, and 100 ml. H2O refluxed 3 hrs. cooled to give 1024 g. free base, m. 165° (C6H6), and refluxed with Me2SO4 in MePh afforded 92% 1-hydroxy-4-(β-methylmorpholinoethylamino)anthraquinone methosulfate (IX). Traces of purpurin (X) in VII modify the true shades of VIII and IX. A mixture of 264 g. V, 1081 g. 4-Me2NC6H4NH2 and 64 g. H3BO4 heated 8 hrs. at 110° under N, cooled, and 4 l. 3% aqueous alc. added, gave 80% 1-hydroxy-2,4-bis(p-dimethylaminoanilino)anthraquinone, m. 225°. Me2SO4 and MeI derivs. were prepared in high yield. The dyes are applied to the hair from aqueous solution at pH 4-9 and 0.05-0.2M concentration The tints obtained were: IV-VII yellow to orange; VIII and IX, violet to purple; Me2SO4 and MeI, gray. The physiol. behavior of the dyes were studied. Aqueous solns. of series II dyes develop unpleasant odors on standing, but not series I and III. The dyes are not eye irritants, and simultaneous bleaching and dyeing is possible. The affinity of the dyes for hair is probably due to the formation of salt bonds with carboxy groups of keratin.

IT 2278-49-1P, Anthraquinone, 1-hydroxy-4-[(3-piperidinopropyl)amino]-
RL: PREP (Preparation)
(preparation of)

RN 2278-49-1 HCAPLUS

CN 9,10-Anthracenedione, 1-hydroxy-4-[[3-(1-piperidinyl)propyl]amino]- (CA INDEX NAME)



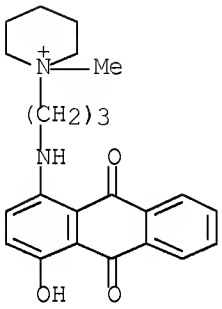
IT 1938-86-9P, Piperidinium, 1-[3-[(9,10-dihydro-4-hydroxy-9,10-dioxo-1-anthracenyl)amino]propyl]-1-methyl-, methyl sulfate (salt)
RL: PREP (Preparation)
(preparation of, and use in dyeing hair)

RN 1938-86-9 HCAPLUS

CN Piperidinium, 1-[3-[(9,10-dihydro-4-hydroxy-9,10-dioxo-1-anthracenyl)amino]propyl]-1-methyl-, methyl sulfate (salt) (9CI) (CA INDEX NAME)

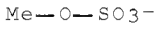
CM 1

CRN 47569-29-9
CMF C23 H27 N2 O3



CM 2

CRN 21228-90-0
CMF C H3 O4 S



Inventor search history

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L19           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L17 AND L18
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L24          51 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND ?ANTHRA?
L25          47 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND ?QUINON?
L26          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 AND L25
L27          18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 OR L21 OR L22 OR L23
L28          43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 OR L26
L32          44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L24 OR L25) AND (?CANCER? OR
                ?TUMOR? OR ?TUMOUR? OR ?CARCIN? OR ?NEOTOM? OR ?NEOPLAS? OR
                ?TOMA?)
L33          57 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 OR L32
L34           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND (?PYRROL? OR ?PIPERIDI
                N?)
L35          57 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 OR L34
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Inventor search results

=> d L35 1-57 ibib ab

L35 ANSWER 1 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:640230 HCAPLUS Full-text
DOCUMENT NUMBER: 149:9894
TITLE: Preparation of N-oxides of cytotoxic heterocyclylalkylaminoanthraquinones as hypoxia-targeting prodrugs in cancer treatment
INVENTOR(S): Pors, Klaus; Phillips, Roger M.; Patterson, Laurence H.
PATENT ASSIGNEE(S): Somanta Limited, UK
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008062252	A1	20080529	WO 2006-IB3389	20061121

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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PRIORITY APPLN. INFO.: WO 2006-IB3389 20061121
OTHER SOURCE(S): MARPAT 149:9894
AB Title compds. e.g. [I; R1-R4 = H, alkyl, halo, OH, alkoxy, aryloxy, acyloxy, NRN(R5)2; R = alkylene; R5 = H, (substituted) alkyl, Q1; ≥1 of R6-R8 = X2, X2-substituted alkyl, the others = H, alkyl; R9 = H, alkyl, X2, X2-substituted alkyl; X2 = halo, OH, alkoxy, aryloxy, acyloxy; ≥1 of R1-R4 = Q1; m = 0, 1; n = 1, 2], were prepared for targeting the hypoxic interior of a cell mass followed by in situ reduction and DNA binding. Thus, title compound 1-[[2-(3-chloropiperidin -1-yl-N-oxide)ethyl]amino]-4-[[(2-dimethylamino-N-oxide)ethyl]amino]-5,8- dihydroxyathracene-9,10-dione (CAQ167MN) was prepared in 62% yield by MCPBA oxidation of the corresponding amine. The title N-oxides penetrated spheroids of HT29 cells and were absent from outer layers of the spheroids.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 2 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:817771 HCAPLUS Full-text
DOCUMENT NUMBER: 147:181530
TITLE: Alkylating anthraquinones for inhibition of pan-cell cycle progression and the treatment of cancer
INVENTOR(S): Epenetos, Agamemnon Antoniou; Pors, Klaus;

Smith, Paul James; Patterson, Laurence H.
PATENT ASSIGNEE(S): Somanta Ltd., UK
SOURCE: PCT Int. Appl., 22pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007083114	A1	20070726	WO 2007-GB140	20070117
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20070208085	A1	20070906	US 2007-655043	20070117
PRIORITY APPLN. INFO.:			US 2006-759693P	P 20060117

OTHER SOURCE(S): MARPAT 147:181530

AB The invention generally relates to chemotherapeutic treatment of proliferative disorders, e.g. cancer. The invention more specifically relates to inhibition of pan-cell cycle progression with alkylating anthraquinones, which may inhibit mitotic commitment, lead to limited expression of G2 arrest and force cells to enter polyploidy via an aberrant mitosis. The methods of the invention are particularly useful in the treatment of chemotherapy-resistant cancers. Examples of compound preparation are included.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 3 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:465870 HCAPLUS Full-text
DOCUMENT NUMBER: 146:454115
TITLE: Examination of the distribution of the bioreductive drug AQ4N and its active metabolite AQ4 in solid tumours by imaging matrix-assisted laser desorption/ionisation mass spectrometry
AUTHOR(S): Atkinson, Sally J.; Loadman, Paul M.; Sutton, Chris; Patterson, Laurence H.; Clench, Malcolm R.
CORPORATE SOURCE: Biomedical Research Centre, Sheffield Hallam University, Sheffield, S1 1WB, UK
SOURCE: Rapid Communications in Mass Spectrometry (2007), 21(7), 1271-1276
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB AQ4N (banoxatrone) (1,4-bis-{[2-(dimethylamino-N-oxide)ethyl]amino}-5,8-dihydroxyanthracene- 9,10-dione) is an example of a bioreductive prodrug in clin. development. In hypoxic cells AQ4N is reduced to the topoisomerase II inhibitor AQ4 (1,4-bis- {[2-(dimethylamino)ethyl]amino}- 5,8-dihydroxyanthracene-9,10-dione). By inhibition of topoisomerase II within these hypoxic areas, AQ4N has been shown to sensitize tumors to existing

chemo- and radiotherapy treatments. In this study the distribution of AQ4N and AQ4 in treated H460 human tumor xenografts has been examined by imaging matrix-assisted laser desorption/ionization mass spectrometry. Images of the distribution of AQ4N and AQ4 have been produced that show little overlap. The distribution of ATP in the tumor xenografts was also studied as an endogenous marker of regions of hypoxia since concns. of ATP are known to be decreased in these regions. The distribution of ATP was similar to that of AQ4N, i.e. in regions of abundant ATP there was no evidence of conversion of AQ4N into AQ4. This indicates that the cytotoxic metabolite AQ4 is confined to hypoxic regions of the tumor as intended.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 4 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1246898 HCAPLUS Full-text
DOCUMENT NUMBER: 146:162991
TITLE: Synthesis of DNA-Directed Pyrrolidinyl and Piperidinyl Confined Alkylating Chloroalkylaminoanthraquinones: Potential for Development of Tumor-Selective N-Oxides
AUTHOR(S): Pors, Klaus; Shnyder, Steven D.; Teesdale-Spittle, Paul H.; Hartley, John A.; Zloh, Mire; Searcey, Mark; Patterson, Laurence H.
CORPORATE SOURCE: Institute of Cancer Therapeutics, University of Bradford, West Yorkshire, BD7 1DP, UK
SOURCE: Journal of Medicinal Chemistry (2006), 49(24), 7013-7023
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:162991

AB A novel series of 1,4-disubstituted chloroethylaminoanthraquinones , containing alkylating chloroethylamino functionalities as part of a rigid piperidinyl or pyrrolidinyl ring-system, have been prepared The target compds. were prepared by ipso-displacement of halides of various anthraquinone chromophores by either hydroxylated or chlorinated piperidinyl- or pyrrolidinylalkylamino side chains. The chloroethylaminoanthraquinones were shown to alkylate guanine residues of linearized pBR322 (1-20 μM), and two sym. 1,4-disubstituted anthraquinones (I, n = 1, 2) were shown to interstrand cross-link DNA in the low nM range. Several 1,4-disubstituted chloroethylaminoanthraquinones were potently cytotoxic (IC50 values: ≤40 nM) in human ovarian cancer A2780 cells. Two agents (II, NR1R2 = 2-chloromethylpyrrolidino, 3- chloropiperidino) exhibited mean GI50 values of 96 nM and 182 nM, resp., in the NCI human tumor cell line panel. Derivatization of the potent DNA crosslinking agent I [n = 2] to an N-oxide resulted in loss of the DNA unwinding, DNA interstrand crosslinking and cytotoxic activity of the parent mol.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 5 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1116881 HCAPLUS Full-text
DOCUMENT NUMBER: 146:269316
TITLE: Spectral analysis of the DNA targeting bisalkylaminoanthraquinone DRAQ5 in intact living cells
AUTHOR(S): Njoh, Kerenza L.; Patterson, Laurence H.; Zloh, Mire; Wiltshire, Marie; Fisher, Janet; Chappell,

Sally; Ameer-Beg, Simon; Bai, Yanhong; Matthews, Daniel; Errington, Rachel J.; Smith, Paul J.
CORPORATE SOURCE: Department of Pathology, School of Medicine, Cardiff University, Cardiff, UK
SOURCE: Cytometry, Part A (2006), 69A(8), 805-814
CODEN: CPAYAV; ISSN: 1552-4922
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: We report on the potential DNA binding modes and spectral characteristics of the cell-permeant far red fluorescent DNA dye, DRAQ5, in solution and bound within intact cells. Our aim was to determine the constraints for its use in flow cytometry and bioimaging. Methods: Solution characteristics and quantum yields were determined by spectroscopy. DRAQ5 binding to nuclear DNA was analyzed using fluorescence quenching of Hoechst 33342 dye, emission profiling by flow cytometry, and spectral confocal laser scanning microscopy of the complex DRAQ5 emission spectrum. Cell cycle profiling utilized an EGFP-cyclin B1 reporter as an independent marker of cell age. Mol. modeling was used to explore the modes of DNA binding. Results: DRAQ5 showed a low quantum yield in solution and a spectral shift upon DNA binding, but no significant fluorescence enhancement. DRAQ5 caused a reduction in the fluorescence intensity of Hoechst 33342 in live cells prelabeled with the UV excitable dye, consistent with mol. modeling that suggests AT preference and an engagement of the minor groove. In vivo spectral anal. of DRAQ5 demonstrated shifts to longer wavelengths upon binding with DNA. Anal. of spectral windows of the dual emission peaks at 681 and 707 nm in cells showed that cell cycle compartment recognition was independent of the far red-near IR emission wavelengths monitored. Conclusions: The study provides new clues to modes of DNA binding of the modified anthraquinone mol. in vivo, and its AT base-pair selectivity. The combination of low quantum yield but high DNA affinity explains the favorable signal-to-noise profile of DRAQ5-nuclear fluorescence. The robust nature of cell cycle reporting using DRAQ5, even when restricted spectral windows are selected, facilitates the anal. of encroaching spectral emissions from other fluorescent reporters, including GFP-tagged proteins.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 6 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:977600 HCAPLUS Full-text
DOCUMENT NUMBER: 145:356561
TITLE: Preparation of analogues of the azinomycins as anti-tumour agents and as prodrugs
INVENTOR(S): Searcey, Mark; Patterson, Laurence, Rylton; Pors, Klaus; Casely-Hayford, Maxwell
PATENT ASSIGNEE(S): School of Pharmacy, University of London, UK
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006097730	A1	20060921	WO 2006-GB941	20060316

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,

MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 1858836 A1 20071128 EP 2006-710103 20060316
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: GB 2005-5644 A 20050318
WO 2006-GB941 W 20060316

OTHER SOURCE(S): CASREACT 145:356561; MARPAT 145:356561

AB Compds. of formula I [X = O, S, (substituted) NH; R1, R2 = H, alkyl, alkoxy, Ph, etc.; R3 = (substituted) NH2, alkylthio, alkoxy, alkyl, OH, etc.] are prepared as oxidation-activated prodrugs. The compds. are expected to be converted into an epoxide at the alkene to which R2 is attached by cytochrome P 450, in particular CYPIBI, expressed at high levels in tumors. The prodrugs are expected to be activated preferentially in tumor cells. Thus, II was prepared, had showed significant antitumor activity against human tumor cell lines.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 7 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:294110 HCAPLUS Full-text
DOCUMENT NUMBER: 145:287817
TITLE: Screening far red probes for use on optical biochip devices
AUTHOR(S): Njoh, Kerenza L.; Patterson, Laurence H.; Pors, Klaus; Zloh, Mire; Ameer-Beg, Simon; Summers, Huw; Matthews, Daniel; Errington, Rachel J.; Smith, Paul J.
CORPORATE SOURCE: Dept. of Pathology, School of Medicine, Cardiff Univ., Cardiff, CF14 4XN, UK
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (2006), 6088(Imaging, Manipulation, and Analysis of Biomolecules, Cells, and Tissues IV), 60880H/1-60880H/11
CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In situ spectral anal. can be used to understand the targeting and interaction of agents in cellular compartments. A range of novel red excitable fluorescent probes, related to the anthraquinone family of anti-cancer agents, were designed for their DNA affinic properties and their ability to enter and penetrate living cells. We report on the spectral features of these probes, both in solution and bound within intact cells, to identify unique fluorescent signatures that exploit their use in bioassays on optical biochip devices. The probes demonstrated red shifted emission spectra and increased 2 photon lifetime, with minimal fluorescent enhancement, upon binding to DNA. Spectral confocal laser scanning microscopy revealed complex emission profiles representing the bound (nuclear) and unbound (cytoplasmic) fractions of the DNA probes within live interphase, mitotic and apoptotic cells. Anal. of the emission peaks encoded the spectra to provide cell compartment recognition and profiles for cells in different cell states. Sampling the entire emission spectra of these probes for cell locating, even in the presence of unbound mols., provides good signal-to-noise in biochip devices. Furthermore, by

sampling the fluorescence output at specific spectral windows we can obtain high spatial information without imaging. The technol. challenge is to integrate these fluorophores and appropriate detection capacity onto an optical biochip platform with microfluidic systems for cell handling.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 8 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:239633 HCAPLUS Full-text
DOCUMENT NUMBER: 144:403932
TITLE: Benzoquinone ansamycin heat shock protein 90 inhibitors modulate multiple functions required for tumor angiogenesis
AUTHOR(S): Sanderson, Sharon; Valenti, Melanie; Gowan, Sharon; Patterson, Lisa; Ahmad, Zahida; Workman, Paul; Eccles, Suzanne A.
CORPORATE SOURCE: Cancer Research UK Centre for Cancer Therapeutics, Institute of Cancer Research, Surrey, UK
SOURCE: Molecular Cancer Therapeutics (2006), 5(3), 522-532
CODEN: MCTOCF; ISSN: 1535-7163
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Heat shock protein 90 (Hsp90) is a mol. chaperone involved in maintaining the correct conformation and stability of its client proteins. This study investigated the effects of Hsp90 inhibitors on client protein expression and key cellular functions required for tumor angiogenesis. The benzoquinone ansamycin Hsp90 inhibitors geldanamycin and/or its derivs. 17-allylamino-17-demethoxygeldanamycin (17-AAG) and 17-(dimethylaminoethylamino)-17-demethoxygeldanamycin inhibited production of vascular endothelial growth factor (VEGF)-A by tumor cells and blocked proliferative responses of human endothelial cells at nanomolar concns. 17-AAG also significantly reduced endothelial cell migration, tubular differentiation, invasion through Matrigel, and secretion of urokinase-type plasminogen activator at concns. at or below those that inhibited proliferation. 17-AAG significantly reduced expression of VEGF receptor (VEGFR)-2 and established Hsp90 client proteins in human endothelial cells in vitro as well as in mouse vena cava, mesenteric vessels, and blood vessels within human tumor xenografts in vivo; this was associated with decreased tumor microvessel d. Finally, we showed for the first time that Hsp90 inhibitors also reduce expression of VEGFR-1 on human vascular endothelial cells, VEGFR-3 on lymphatic endothelial cells in vitro, and all three VEGFRs on mouse vasculature in vivo. Thus, we identify Hsp90 inhibitors as important regulators of many aspects of tumor angiogenesis (and potentially lymph angiogenesis) and suggest that they may provide therapeutic benefit not only via direct effects on tumor cells but also indirectly by inhibiting the production of angiogenic cytokines and responses of activated endothelial cells that contribute to tumor progression and metastasis.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 9 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1178618 HCAPLUS Full-text
DOCUMENT NUMBER: 143:378940
TITLE: DNA mismatch repair deficiency, resistance to cancer chemotherapy and the development of hypersensitive agents
AUTHOR(S): Pors, Klaus; Patterson, Laurence H.
CORPORATE SOURCE: Institute of Cancer Therapeutics, University of Bradford, West Yorkshire, BD7 1DP, UK
SOURCE: Current Topics in Medicinal Chemistry (Sharjah, United

Arab Emirates) (2005), 5(12), 1133-1149
CODEN: CTMCCL; ISSN: 1568-0266
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. DNA Mismatch Repair (MMR) deficiency results in resistance to platinating and alkylating agents, DNA minor groove binders, inhibitors of topoisomerases and antimetabolites. The cellular MMR pathway, involving hMLH1 and MSH2, detects and repairs DNA frame shifts replication errors and regulates recombination events. Tumor cells are able to cope with DNA damage caused by chemotherapy as long as the MMR-process is disabled and hence there is a need to develop agents that (i) restore MMR proficiency or (ii) are hypersensitive in cells that are irreversibly MMR deficient. Decitabine is suggested to restore MMR function by reversal of gene promoter hypermethylation of hMLH1. However, when MMR is deficient due to gene mutation it is not feasible to design agents, since the absence of functional proteins that constitute the MMR machinery are not available as targets. The evidence that resistance to chemotherapy is associated with hMSH2 and/or hMLH1 deficiency has revealed a new paradigm for drug discovery of agents that pos. exploit this phenotype to therapeutic advantage. Even more attractive is the development of agents that are hypersensitive in the absence of functional MMR to enable even more effective treatment. In this regard, established agents such as mitomycin C, camptothecin or novel hydroxyethylaminoanthraquinones may represent opportunities for exploitation of MMR-deficiency in tumor cells.
REFERENCE COUNT: 136 THERE ARE 136 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 10 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1015902 HCAPLUS Full-text
DOCUMENT NUMBER: 143:459905
TITLE: Design and synthesis of a DNA-crosslinking azinomycin analogue
AUTHOR(S): Casely-Hayford, Maxwell A.; Pors, Klaus; James, Colin H.; Patterson, Laurence H.; Hartley, John A.; Searcey, Mark
CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry, School of Pharmacy, University of London, London, WC1N 1AX, UK
SOURCE: Organic & Biomolecular Chemistry (2005), 3(19), 3585-3589
CODEN: OBCRAK; ISSN: 1477-0520
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:459905
AB The azinomycins are potent antitumor antibiotics that are able to crosslink DNA, but are relatively unstable and unlikely to progress as therapeutic candidates. A prototype analog I (R = Cl) with more clin. potential has been designed and synthesized and incorporates the epoxide function of the azinomycins and a nitrogen mustard. Two further analogs I (R = OH) and II that can alkylate DNA but cannot crosslink the duplex have also been synthesized. Compound I (R = Cl) crosslinks DNA efficiently at nM concns. Compds. I (R = Cl, OH) and II were submitted to the NCI 60 cell line screen and have similar antitumor activity, although I (R = Cl) is slightly less active than the non-crosslinking compds. These observations will be important in the design of further azinomycin analogs with antitumor activity.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 11 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1008901 HCAPLUS Full-text
DOCUMENT NUMBER: 143:440042
TITLE: Development of Nonsymmetrical 1,4-Disubstituted Anthraquinones That Are Potently Active against Cisplatin-Resistant Ovarian Cancer Cells
AUTHOR(S): Pors, Klaus; Plumb, Jane A.; Brown, Robert; Teesdale-Spittle, Paul; Searcey, Mark; Smith, Paul J.; Patterson, Laurence H.
CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry, The School of Pharmacy, University of London, London, WC1N 1AX, UK
SOURCE: Journal of Medicinal Chemistry (2005), 48(21), 6690-6695
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:440042
AB A novel series of 1,4-disubstituted aminoanthraquinones were prepared by ipso-displacement of 1,4-difluoro-5,8- dihydroxyanthraquinones by hydroxylated piperidinyl- or pyrrolidinylalkylamino side chains. The compds. were evaluated in the A2780 ovarian cancer cell line and its cisplatin-resistant variants (A2780/cp70 and A2780/MCP1). The novel anthraquinones were shown to possess up to 5-fold increased potency against the cisplatin-resistant cells compared to the wild-type cells. Growth curve anal. of the hydroxyethylaminoanthraquinone I in the osteosarcoma cell line U-2 OS showed that the cell cycle is not frozen, rather there is a late cell cycle arrest consistent with the action of a DNA-damaging topoisomerase II inhibitor. Accumulative apoptotic events, using time lapse photog., indicate that I is capable of fully engaging cell cycle arrest pathways in G2 in the absence of early apoptotic commitment. I and its chloro analog retained significant activity against human A2780/cp70 xenografted tumors in mice.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 12 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:588893 HCAPLUS Full-text
DOCUMENT NUMBER: 143:115360
TITLE: A preparation of anthraquinone derivatives, useful as antitumor agents
INVENTOR(S): Patterson, Laurence Hylton; Pors, Klaus; Teesdale-Spittle, Paul Henry
PATENT ASSIGNEE(S): School of Pharmacy, University of London, UK
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005061453	A1	20050707	WO 2004-GB5390	20041222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004303592	A1	20050707	AU 2004-303592		20041222
CA 2550839	A1	20050707	CA 2004-2550839		20041222
EP 1701939	A1	20060920	EP 2004-806187		20041222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS					
CN 1934079	A	20070321	CN 2004-80041751		20041222
JP 2007516270	T	20070621	JP 2006-546313		20041222
IN 2006DN03556	A	20070810	IN 2006-DN3556		20060620
US 20080027107	A1	20080131	US 2007-596783		20070208
PRIORITY APPLN. INFO.:			GB 2003-29820	A	20031223
			GB 2003-30011	A	20031224
			WO 2004-GB5390	W	20041222

OTHER SOURCE(S): CASREACT 143:115360; MARPAT 143:115360

AB The invention relates to a preparation of anthraquinone derivs. of formula I [wherein: R1 to R4 are each selected from H, alkyl, halogen, NH-alkanediyl-heterocycle, or OH, etc.], useful as antitumor agents. For instance, anthraquinone derivative II (inhibition of cell growth: IC50 = 8.4 nM) was prepared via amination of fluoroanthracene derivative III by [1-(2-aminoethyl)piperidin -3-yl]methanol with a yield of 68%.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 13 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:191748 HCAPLUS Full-text

TITLE: Design, synthesis and biological evaluation of potential anticancer agents based on the azinomycins

AUTHOR(S): Casely-Hayford, Maxwell A.; Pors, Klaus; Patterson, Laurence H.; Searcey, Mark

CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry, The School of Pharmacy, University of London, London, WC1N 1AX, UK

SOURCE: Abstracts of Papers, 229th ACS National Meeting, San Diego, CA, United States, March 13-17, 2005 (2005), MEDI-415. American Chemical Society: Washington, D. C.
CODEN: 69GQMP

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Azinomycins A and B are extremely potent antitumor antibiotics that derive their activity from the alkylation of duplex DNA at GXN. At the time of isolation, compound 1, which constitutes the left hand portion of the parent azinomycins, was also discovered and was later shown to possess significant cytotoxicity. Due to our continuing interest in potential bioreductive drugs, and in the design and synthesis of DNA-binding antitumor agents, we synthesized compound 2, an analog of 1 that contains a piperidine mustard. The alkylating group-chromophore distance is similar to that found in the natural product and is connected to the chromophore by a more robust amide bond. Synthesis of the target mol. and a non-alkylating analog was successfully achieved and the resulting compound shown to bind to and alkylate DNA in a similar fashion to the natural product. Analogs of 2 with differing mustard functions are also under development.

L35 ANSWER 14 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:74677 HCAPLUS Full-text
DOCUMENT NUMBER: 142:279977
TITLE: Truncated azinomycin analogues intercalate into DNA
AUTHOR(S): Casely-Hayford, Maxwell A.; Pors, Klaus; Patterson, Laurence H.; Gerner, Clive; Neidle, Stephen; Searcey, Mark
CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry, School of Pharmacy, University of London, London, WC1N 1AX, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(3), 653-656
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:279977
AB The design and synthesis of a potentially more therapeutically-viable azinomycin analog I was completed. It involved coupling of a piperidine mustard to the acid chloride of the azinomycin chromophore. Both the designed azinomycin analog I and the natural product bind to DNA and cause unwinding, supporting an intercalative mode of binding.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 15 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:158152 HCAPLUS Full-text
DOCUMENT NUMBER: 140:357040
TITLE: Synthesis and Biological Evaluation of Novel Chloroethylaminoanthraquinones with Potent Cytotoxic Activity against Cisplatin-Resistant Tumor Cells
AUTHOR(S): Pors, Klaus; Paniwnyk, Zennia; Ruparelia, Ketan C.; Teesdale-Spittle, Paul H.; Hartley, John A.; Kelland, Lloyd R.; Patterson, Laurence H.
CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry, School of Pharmacy, University of London, London, WC1N 1AX, UK
SOURCE: Journal of Medicinal Chemistry (2004), 47(7), 1856-1859
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:357040
AB Novel 1- and 1,4-substituted chloroethylaminoanthraquinones with DNA binding and alkylating properties along with their resp. hydroxyethylaminoanthraquinone intermediates were synthesized. Selected chloroethylaminoanthraquinones were shown to cross-link DNA and alkylate guanines (at low nM concentration) with a preference for reaction sites containing 5'-PyG. A compound (Alchemix) with the bis-chloroethyl functionality confined to one side chain alkylated but did not cross-link DNA. All the 1,4-disubstituted chloroethylaminoanthraquinones were potently cytotoxic (nM IC50s) against cisplatin-resistant ovarian cancer cell lines.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 16 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:757670 HCAPLUS Full-text
DOCUMENT NUMBER: 139:281237

TITLE: Formulations of anthraquinone derivatives
INVENTOR(S): Denny, William Alexander; Patterson, Laurence Hylton; Halbert, Gavin William; Ford, Steven John
PATENT ASSIGNEE(S): BTG International Limited, UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078387	A1	20030925	WO 2003-GB1110	20030317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2478867	A1	20030925	CA 2003-2478867	20030317
AU 2003212534	A1	20030929	AU 2003-212534	20030317
EP 1485349	A1	20041215	EP 2003-708354	20030317
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006501140	T	20060112	JP 2003-576395	20030317
ZA 2004007021	A	20060628	ZA 2004-7021	20040902
MX 2004PA08821	A	20041126	MX 2004-PA8821	20040910
US 20050256188	A1	20051117	US 2004-507483	20040927
US 7074835	B2	20060711		
US 20060205820	A1	20060914	US 2006-433545	20060515
US 7276537	B2	20071002		

PRIORITY APPLN. INFO.:		
GB 2002-6255	A	20020315
US 2002-412776P	P	20020924
WO 2003-GB1110	W	20030317
US 2004-507483	A1	20040927

OTHER SOURCE(S): MARPAT 139:281237

AB An anthraquinone derivative is formulated so that upon dissoln. in aqueous solution the pH of the solution is in the range of 5 to 9. The compound may be in the form of salt with a physiol. acceptable acid having a pKa in the range of -3.0 (minus 3.0) to 9.0. For example, to 10 mg of an anthracenedione derivative AQ4N, dissolved in 1 mL of MeOH, 73.7 mg of pimelic acid, dissolved in 1 mL of MeOH, was added to yield 8.2 mg (47%) of AQ 4N dipimelate. Also, an anthraquinone derivative AQMN had a cytotoxicity which is at least 5 times greater than that of AQ 4N in the P388 system.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 17 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:655735 HCAPLUS Full-text
DOCUMENT NUMBER: 140:122227
TITLE: Alchemix: A novel alkylating anthraquinone with potent activity against anthracycline- and cisplatin-resistant ovarian cancer
AUTHOR(S): Pors, Klaus; Paniwnyk, Zennia; Teesdale-Spittle, Paul; Plumb, Jane A.;

Willmore, Elaine; Austin, Caroline A.; Patterson, Laurence H.
CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry, The School of Pharmacy, University of London, London, WC1N 1AX, UK
SOURCE: Molecular Cancer Therapeutics (2003), 2(7), 607-610
CODEN: MCTOCF; ISSN: 1535-7163
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chloroethylaminoanthraquinones are described with intercalating and alkylating capacity that potentially covalently cross-link topoisomerase II (topo II) to DNA. These compds. have potent cytotoxic activity (IC50 = 0.9-7.6 nM) against the A2780 human ovarian carcinoma cell line. Hydroxyethylaminoanthraquinones also reported in this paper have similar IC50 values (0.7-1.7 nM) in the same cell line. Alchemix (ZP281M, 1-{2-[N,N-bis(2- chloroethyl)amino]ethylamino}-4-{2- [N,N-(dimethyl)amino]ethylamino}-5,8- dihydroxy-9,10-anthracenedione), an alkylating anthraquinone, retains excellent antitumor activity in Adriamycin-resistant (2780AD) and cisplatin-resistant (2780/cp70) cell lines in vitro and in vivo. This indicates that Alchemix can evade both P-glycoprotein efflux pump and DNA mismatch repair-mediated resistance. In treated cells, Alchemix was shown to preferentially induce drug-stabilized covalent bound topo IIα-DNA complexes over topo IIβ-DNA complexes.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 18 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:733727 HCAPLUS Full-text
DOCUMENT NUMBER: 138:296878
TITLE: Bioreductively activated antitumor N-oxides: the case of AQ4N, a unique approach to hypoxia-activated cancer chemotherapy
AUTHOR(S): Patterson, Laurence H.
CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry, School of Pharmacy, University of London, London, WC1N 1AX, UK
SOURCE: Drug Metabolism Reviews (2002), 34(3), 581-592
CODEN: DMTRAR; ISSN: 0360-2532
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Aliphatic amine N-oxides have long been identified as non-toxic metabolites of a large number of tertiary amine drugs. Bioredn. of such N-oxides will generate the active parent amine. This principle has been adopted to develop AQ4N, a di-N-oxide anticancer prodrug with little intrinsic cytotoxicity. However, AQ4N is bioreduced in hypoxic regions of solid tumors and micro-metastatic deposits to generate a cytotoxic alkylaminoanthraquinone metabolite. The 4-electron reduction metabolite of AQ4N has high affinity for DNA and is a potent inhibitor of topoisomerase II, a DNA processing enzyme crucial to cell division. The development of AQ4N has proceeded on many fronts in order to establish this unique anticancer prodrug opportunity. Preclin. studies in vivo have demonstrated that although AQ4N has little or no intrinsic cytotoxic activity per se it (i) enhances the antitumor effects of radiation and conventional chemotherapeutic agents, (ii) is pharmacokinetically stable, and (iii) is a substrate for cytochrome P 450 (CYP). A study of AQ4N metabolism in vitro and ex vivo using purified CYP enzymes, phenotyped human livers and CYP transfected cell lines shows that CYP3A, 1A and 1B1 family members contribute to AQ4N bioredn. in the absence of oxygen. Importantly AQ4N is shown to be metabolized by tumors known to express CYP isoforms. AQ4N is currently in Phase I clin. trials.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 19 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:430670 HCAPLUS Full-text
DOCUMENT NUMBER: 137:345402
TITLE: Tumor cytochrome P450 and drug activation
AUTHOR(S): Patterson, L. H.; Murray, G. I.
CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry, The School of Pharmacy, University of London, London, WC1N 1AX, UK
SOURCE: Current Pharmaceutical Design (2002), 8(15), 1335-1347
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The expression of drug-metabolizing cytochrome P450s (CYPs), notably 1A, 1B, 2C, 3A, 2D, has been identified in a wide range of human cancers. Individual tumor types have distinct CYP profiles as studied by detection of CYP activity, identification of immunoreactive CYP protein and detection of CYP mRNA. Selected CYPs, especially CYP1B1, are overexpressed in tumors including cancers of the lung, breast, liver, gastrointestinal tract, prostate, bladder. Several prodrug antitumor agents have retrospectively been identified as CYP substrates for which tumor CYP activation may hitherto have been underestimated. Those in clin. use include prodrug alkylating agents (cyclophosphamide, ifosphamide, dacarbazine, procarbazine), Tegafur (a prodrug fluoropyrimidine), and methoxymorpholinodoxorubicin (a metabolically activated anthracycline), as well as flutamide and tamoxifen, two nonsteroidal hormone receptor antagonists that are significantly more active following hydroxylation by CYP. More exciting is the prospect of developing new agents designed to be selectively dependent on activation by tumor CYPs. This is illustrated by activation of the 2-(4-aminophenyl)benzothiazoles exclusively in tumors with inducible CYP1A1. Also of interest is the bioreductive antitumor prodrug AQ4N, a CYP3A substrate that is activated to a cytotoxic metabolite specifically in hypoxic tumor regions.
REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 20 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:503379 HCAPLUS Full-text
DOCUMENT NUMBER: 135:313275
TITLE: Involvement of NADPH: cytochrome P450 reductase in the activation of indoloquinone EO9 to free radical and DNA damaging species
AUTHOR(S): Bailey, S. M.; Lewis, A. D.; Patterson, L. H. ; Fisher, G. R.; Knox, R. J.; Workman, P.
CORPORATE SOURCE: CRC Beatson Laboratories, CRC Department of Medical Oncology, Garscube Estate, Bearsden, Glasgow, G61 1BD, UK
SOURCE: Biochemical Pharmacology (2001), 62(4), 461-468
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Evidence suggests that DT-diaphorase is involved in the activation and mechanism of cytotoxicity of the investigational indoloquinone anticancer drug EO9 under aerobic conditions. Data also implicate a role for other enzymes including NADPH: cytochrome P 450 reductase, especially in low DT-diaphorase tumor cells and under hypoxic conditions. Here, the authors used purified rat NADPH: cytochrome P 450 reductase to provide addnl. evidence in support of a

role for this enzyme in activation of EO9 to generate free radical and DNA-damaging species. ESR spectrometry studies showed that NADPH: cytochrome P 450 reductase reduced EO9 to a free radical species, including a drug radical (most likely the semiquinone) and reactive oxygen species. Plasmid DNA expts. showed that reduction of EO9 catalyzed by NADPH: cytochrome P 450 reductase results in single-strand breaks in DNA. The information obtained may contribute to the understanding of the mol. mechanism of DNA damage and cytotoxicity exerted by EO9 and may be useful in the design of future bioreductive drugs.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 21 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:266493 HCAPLUS Full-text
DOCUMENT NUMBER: 135:174632
TITLE: A preclinical pharmacokinetic study of the bioreductive drug AQ4N
AUTHOR(S): Loadman, P. M.; Swaine, D. J.; Bibby, M. C.; Welham, K. J.; Patterson, L. H.
CORPORATE SOURCE: Cancer Research Unit, University of Bradford, Bradford, BD7 1DP, UK
SOURCE: Drug Metabolism and Disposition (2001), 29(4, Pt. 1), 422-426
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB AQ4N (1,4-bis-{[2-(dimethylamino-N-oxide)ethyl]amino}5,8- dihydroxyanthracene-9,10-dione) is in a class of bioreductive agents incorporating the aliphatic N-oxide functionality and is well documented as a very effective enhancer of radiotherapy and chemotherapy. The compound is shortly to enter Phase I clin. trials in the United Kingdom, and this study describes the preclin. pharmacokinetics and metabolism of AQ4N in mice. AQ4N was administered by i.v. injection at doses of 200, 100, and 20 mg/kg and was quantified by high-performance liquid chromatog. and liquid chromatog./mass spectroscopy. There was a linear increase in the maximum plasma concentration (Cmax) proportional to dose with a Cmax of 1171 μg/mL at the maximum tolerated dose of 200 mg/kg. The area under plasma concentration vs. time curve (AUC) increased disproportionately with dose from 14.1 μg/h/mL at 20 mg/kg to 247 μg/h/mL at 200 mg/kg with a subsequent decrease in clearance. Terminal elimination half-lives ranged from 0.64 to 0.83 h. The spectra of the two major metabolites matched those from authentic stds. with the mol. ions [M + H]+ being detected at m/z 445.4 (AQ4N), m/z 429.5 (AQ4 mono-N-oxide) and m/z 413.5 (AQ4). Only low concns. of the toxic metabolite (AQ4) were detected in plasma at all 3 doses, with the AUC and Cmax at 200 mg/kg being 3.54 μg/h/mL and 3.7 μg/mL, resp., representing <2% of AQ4N. Concns. of the intermediate AQ4 M represented 8, 10, and 18% of those for AQ4N at the doses of 20,100, and 200 mg/kg. The concns. necessary for a therapeutic response in vivo have been described in this pharmacokinetic study.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 22 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:118618 HCAPLUS Full-text
DOCUMENT NUMBER: 134:266560
TITLE: Anthraquinone-peptides as inhibitors of AP-1 transcription factor
AUTHOR(S): Ijaz, T.; Tran, P.; Ruparelia, K. C.;

Teesdale-Spittle, P. H.; Orr, S.; Patterson, L. H.

CORPORATE SOURCE: School of Pharmacy & Pharmaceutical Sciences, De Montfort University, Leicester, LE1 9BH, UK

SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(3), 351-353
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Anthraquinone-peptide conjugates I (peptide = ARCKA, AKCRA, AKSRA, AKCRNA, AKCRKA, AKCRNRA, AKCRKRA, AAKCRAA; A = Ala, R = Arg, C = Cys, K = Lys, S = Ser, N = Asn), containing 5-7 amino acids including the KCR motif important in AP-1 protein binding to DNA, have been synthesized as potential transcription factor inhibitors. I showed DNA intercalative binding and inhibition of AP-1 protein binding to its DNA consensus sequence.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 23 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:592260 HCAPLUS Full-text

DOCUMENT NUMBER: 134:204641

TITLE: Characteristics of a novel deep red/infrared fluorescent cell-permeant DNA probe, DRAQ5, in intact human cells analyzed by flow cytometry, confocal and multiphoton microscopy

AUTHOR(S): Smith, Paul J.; Blunt, Nicola; Wiltshire, Marie; Hoy, Terence; Teesdale-Spittle, Paul; Craven, Michael R.; Watson, James V.; Amos, W. Brad; Errington, Rachel J.; Patterson, Laurence H.

CORPORATE SOURCE: Department of Pathology, University of Wales College of Medicine, Cardiff, CF4 4XN, UK

SOURCE: Cytometry (2000), 40(4), 280-291
CODEN: CYTODQ; ISSN: 0196-4763
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: The multiparameter fluorometric anal. of intact and fixed cells often requires the use of a nuclear DNA discrimination signal with spectral separation from visible range fluorochromes. We have developed a novel deep red fluorescing bisalkylaminoanthraquinone, DRAQ5 (Exλmax 646 nm; Emλmax 681 nm; Emλrange 665->800 nm), with high affinity for DNA and a high capacity to enter living cells. We describe here the spectral characteristics and applications of this synthetic compound, particularly in relation to cytometric anal. of the cell cycle. Methods: Cultured human tumor cells were examined for the ability to nuclear locate DRAQ5 using single and multiphoton laser scanning microscopy (LSM) and multiparameter flow cytometry. Results: Multiparameter flow cytometry shows that the dye can rapidly report the cellular DNA content of live and fixed cells at a resolution level adequate for cell cycle anal. and the cycle-specific expression of cellular proteins (e.g., cyclin B1). The preferential excitation of DRAQ5 by laser red lines (633/647 nm) was found to offer a means of fluorescence signal discrimination by selective excitation, with greatly reduced emission overlap with UV-excitable and visible range fluophors as compared with propidium iodide. LSM reveals nuclear architecture and clearly defines chromosomal elements in live cells. DRAQ5 was found to permit multiphoton imaging of nuclei using a 1,047-nm emitting mode-locked YLF laser. The unusual spectral properties of DRAQ5 also permit live cell DNA anal. using conventional 488 nm excitation and the single-photon imaging of nuclear fluorescence using laser excitation between 488 nm and low IR (IR; 780 nm) wavelengths. Single and multiphoton microscopy

studies revealed the ability of DRAQ5 to report three-dimensional nuclear structure and location in live cells expressing endoplasmic reticulum targeted-GFP, Mito-Tracker-stained mitochondria, or a vital cell probe for free zinc (Zinquin). Conclusion: The fluorescence excitation and emission characteristics of DRAQ5 in living and fixed cells permit the incorporation of the measurement of cellular DNA content into a variety of multiparameter cytometric analyses.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 24 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:456931 HCAPLUS Full-text
DOCUMENT NUMBER: 133:89340
TITLE: Preparation of anthraquinone anticancer drugs
INVENTOR(S): Potter, Gerard Andrew; Patterson, Laurence Hylton; Teesdale-Spittle, Paul; Paniwynk, Zennia
PATENT ASSIGNEE(S): Demontfort University, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038734	A1	20000706	WO 1999-GB4158	19991209
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356399	A1	20000706	CA 1999-2356399	19991209
EP 1140200	A1	20011010	EP 1999-959561	19991209
EP 1140200	B1	20021113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533418	T	20021008	JP 2000-590685	19991209
AT 227588	T	20021115	AT 1999-959561	19991209
PT 1140200	T	20030331	PT 1999-959561	19991209
AU 759549	B2	20030417	AU 2000-16701	19991209
AU 2000016701	A	20000731		
ES 2188273	T3	20030616	ES 1999-959561	19991209
US 6465522	B1	20021015	US 2001-868956	20011107
PRIORITY APPLN. INFO.:			GB 1998-28670 A	19981224
			WO 1999-GB4158 W	19991209

OTHER SOURCE(S): MARPAT 133:89340
AB The title compds. [I; X = halo, substituted sulfonate group; m = 1-5; n = 1-5; NR1R2 is primary, secondary or tertiary, or in the N-oxide form (NOR1R2)], useful in the treatment of cancers such as ovarian cancer, were prepared E.g., a multi-step synthesis of I [X = Cl; n = 1; m = 1; R1, R2 = Me] which showed IC50 of 0.49 μM in drug resistant ovarian cancer cell line SKOV-3, was given.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 25 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:444226 HCAPLUS Full-text
DOCUMENT NUMBER: 133:305336
TITLE: Enhancement of chemotherapy and radiotherapy of murine tumors by AQ4N, a bioreductively activated anti-tumor agent
AUTHOR(S): Patterson, L. H.; McKeown, S. R.; Ruparelia, K.; Double, J. A.; Bibby, M. C.; Cole, S.; Stratford, I. J.
CORPORATE SOURCE: School of Pharmacy and Pharmaceutical Sciences, De Montfort University, Leicester, LE1 9BH, UK
SOURCE: British Journal of Cancer (2000), 82(12), 1984-1990
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Harcourt Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AQ4 (1,4-Bis-{[2-(dimethylamino-N-oxide)ethyl]amino}5,8- dihydroxyanthracene-9, 10-dione) is a prodrug designed to be excluded from cell nuclei until bioreduced in hypoxic cells to AQ4, a DNA intercalator and topoisomerase II poison. Thus, AQ4N is a highly selective bioreductive drug that is activated in, and is preferentially toxic to, hypoxic cells in tumors. Five murine tumors (MAC16, MAC26, NT, SCCVII and RIF-1) have been used to investigate the anti-tumor effects of AQ4N. In only one tumor (MAC16) was AQ4N shown to be active as a single agent. However, when combined with methods to increase the hypoxic tumor fraction in RIF-1 (by phys. clamping) and MAC26 tumors (using hydralazine) there was a substantial enhancement in anti-tumor effect. Notably, RIF-1 tumors treated with AQ4N (250 mg kg-1) followed 15 min later by phys. occluding the blood supply to the tumor for 90 min, resulted in a 13-fold increase in growth delay. When combined with radiation or chemotherapy, AQ4N substantially increased the effectiveness of these modalities in a range of in vivo model systems. AQ4N potentiates the action of radiation in both a drug and radiation dose-dependent manner. Further the enhancement observed is schedule-independent with AQ4N giving similar effects when given at any time within 16 h before or after the radiation treatment. In combination with chemotherapy it is shown that AQ4N potentiates the activity of cyclophosphamide, cisplatin and thiotepa. Both the chemotherapeutic drugs and AQ4N are given at doses which individually are close to their estimated maximum tolerated dose (data not included) which provides indirect evidence that in the combination chemotherapy expts. there is some tumor selectivity in the enhanced action of the drugs.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 26 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:377582 HCAPLUS Full-text
DOCUMENT NUMBER: 133:144412
TITLE: High-performance liquid chromatographic analysis of AQ4N, an alkylaminoanthraquinone N-oxide
AUTHOR(S): Swaine, D. J.; Loadman, P. M.; Bibby, M. C.; Graham, M. A.; Patterson, L. H.
CORPORATE SOURCE: Clinical Oncology Unit, University of Bradford, Bradford, West Yorkshire, BD7 1DP, UK
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2000), 742(2), 239-245
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple, highly selective and reproducible reversed-phase high-performance liquid chromatog. method has been developed for the anal. of the new anti-cancer pro-drug AQ4N. The sample pre-treatment involves a simple protein precipitation protocol, using methanol. Chromatog. sepns. were performed using a HiChrom HIRPB (25 cm+4.6 mm I.D.) column, with mobile phase of acetonitrile-ammonium formate buffer (0.05 M) (22:78, volume/volume), with final pH adjusted to 3.6 with formic acid. The flow-rate was maintained at 1.2 mL min-1. Detection was via photodiode array performed in the UV range at 242 nm and, since the compds. are an intense blue color, in the visible range at 612 nm. The structurally related compound mitoxantrone was used as internal standard The validated quantification range of the method was 0.05-10.0 μg ml-1 in mouse plasma. The inter-day relative standard deviations (RSDs) (n=5) ranged from 18.4% and 12.1% at 0.05 μg ml-1 to 2.9% and 3.3% at 10.0 μg ml-1 for AQ4N and AQ4, resp. The intra-day RSDs for supplemented mouse plasma (n=6) ranged from 8.2% and 14.2% at 0.05 μg ml-1 to 7.6% and 11.5% at 10.0 μg ml-1 for AQ4N and AQ4, resp. The overall recovery of the procedure for AQ4N was 89.4±1.77% and 76.1±7.26% for AQ4. The limit of detection was 50 ng ml-1 with a 100 μl sample volume The method described provides a suitable technique for the future anal. of low levels of AQ4N and AQ4 in clin. samples.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 27 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:811319 HCAPLUS Full-text
DOCUMENT NUMBER: 132:51150
TITLE: 1,5-Bis[2-(dimethylamino)ethyl]-4,8-dihydroxyanthracene-9,10-dione, its di-N,N'-dioxide, its production and its use as a DNA fluorescent dye
INVENTOR(S): Smith, Paul James; Patterson, Laurence Hylton
PATENT ASSIGNEE(S): University of Wales College of Medicine, UK; De Montfort University
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965992	A1	19991223	WO 1999-GB1904	19990615
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2340670	A1	19991223	CA 1999-2340670	19990615
AU 9943804	A	20000105	AU 1999-43804	19990615
AU 771378	B2	20040318		
EP 1086178	A1	20010328	EP 1999-926619	19990615
EP 1086178	B1	20030903		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2002531587	T	20020924	JP 2000-554804	19990615
AT 248897	T	20030915	AT 1999-926619	19990615
PT 1086178	T	20040130	PT 1999-926619	19990615
ES 2207232	T3	20040516	ES 1999-926619	19990615
US 6468753	B1	20021022	US 2001-719863	20010220
US 20030008316	A1	20030109	US 2002-215945	20020812
US 7060427	B2	20060613		

US 20060148777	A1	20060706	US 2006-367328		20060306
PRIORITY APPLN. INFO.:			GB 1998-13062	A	19980618
			WO 1999-GB1904	W	19990615
			US 2001-719863	A3	20010220
			US 2002-215945	A3	20020812

OTHER SOURCE(S): MARPAT 132:51150

AB The fluorescent anthraquinone dye 1,5-bis[2- (dimethylamino)ethyl]-4,8-dihydroxyanthracene-9,10-dione (I) and its dioxide are obtained for use in fluorescence detection technologies with DNA. In an example, I was prepared from 1,5- dichloroanthraquinone and N,N-dimethylethylenediamine, the intermediate product being treated with NaClO3 and NaHSO3 to effect hydroxylation. Flow cytometry was used to illustrate applications of I and its N,N'-dioxide.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 28 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:791736 HCAPLUS Full-text

DOCUMENT NUMBER: 132:75584

TITLE: A novel cell permeant and far red-fluorescing DNA probe, DRAQ5, for blood cell discrimination by flow cytometry

AUTHOR(S): Smith, Paul J.; Wiltshire, Marie; Davies, Sharon; Patterson, Laurence H.; Hoy, Terence

CORPORATE SOURCE: Department of Pathology, College of Medicine, University of Wales, Cardiff, CF4 4XN, UK

SOURCE: Journal of Immunological Methods (1999), 229(1-2), 131-139
CODEN: JIMMBG; ISSN: 0022-1759

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The deep red fluorescing agent (DRAQ5) is a synthetic anthraquinone with a high affinity for DNA and a high capacity to rapidly enter living cells or stain fixed cells. DRAQ5 is optimally excited by red-light emitting sources and yields a deep red emission spectrum which extends into the low infra-red. DRAQ5 shows excitation at sub-optimal wavelengths including the 488 nm line and the multi-line UV wavelengths emitted by argon-ion lasers. Single beam (488 nm) flow cytometry has been used to demonstrate the utility of DRAQ5-nuclear DNA fluorescence as a discriminating parameter for human leukocytes and lymphoma cells, in combination with fluorochrome-labeled antibodies for the detection of surface antigens and subpopulation recognition. DRAQ5 fluorescence was found to reflect cellular DNA content as evidenced by cell cycle distribution profiles for asynchronous and cell cycle-perturbed populations. Importantly, DRAQ5 can be used in combination with FITC and RPE-labeled antibodies, without the need for fluorescence compensation.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 29 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:769512 HCAPLUS Full-text

DOCUMENT NUMBER: 132:87720

TITLE: Rat cytochromes P450 (CYP) specifically contribute to the reductive bioactivation of AQ4N, an alkylaminoanthraquinone-di-N-oxide anticancer prodrug

AUTHOR(S): Raleigh, S. M.; Wanogho, E.; Burke, M. D.; Patterson, L. H.

CORPORATE SOURCE: School of Pharmacy & Pharmaceutical Sciences, De Montfort University, Leicester, LE1 9BH, UK

SOURCE: Xenobiotica (1999), 29(11), 1115-1122
CODEN: XENOBH; ISSN: 0049-8254
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The bioreductive activation of the alkylaminoanthraquinone di-N-oxide prodrug AQ4N has been characterized in rat hepatic tissue using HPLC. AQ4N was shown to be metabolized to two products, namely AQM, the two electron reduced mono-N-oxide, and AQ4, the four electron reduced active cytotoxic agent. Metabolism was shown to occur in microsomes with an apparent Km = 30.29 μM and Vmax = 1.05 nmol/mg/min. Bioredn. was dependent on anaerobic conditions and the presence of the reduced cofactor NADPH. Ketoconazole (100 μM) and carbon monoxide both inhibited AQ4N metabolism inferring a role for cytochrome P 450 (CYP). Microsomes from phenobarbitone and isoniazid-pretreated animals significantly ($p < 0.05$) enhanced the formation of AQ4 from AQ4N indicating a role for CYP2B and 2E resp. The involvement of both CYP2B and 2E was confirmed by the use of CYP-specific inhibitors. In conclusion, the involvement of rat hepatic CYP in the reductive bioactivation of the novel antitumor prodrug AQ4N has been established in detail for the first time. These findings highlight an important interspecies difference between the metabolism of AQ4N in rat and man which was shown earlier to be mediated by CYP3A enzymes. The pharmacol. significance of this is discussed.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 30 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:703964 HCAPLUS Full-text
DOCUMENT NUMBER: 132:75438
TITLE: Effects of AQ4N and its reduction product on radiation-mediated DNA strand breakage
AUTHOR(S): Mohsin Ali, M.; Symons, M. C. R.; Taiwo, F. A.; Patterson, L. H.
CORPORATE SOURCE: Institute of Nuclear Science and Technology, Atomic Energy Research Establishment, Dhaka, Bangladesh
SOURCE: Chemico-Biological Interactions (1999), 123(1), 1-10
CODEN: CBINA8; ISSN: 0009-2797
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Supercoiled plasmid pBR322 DNA was irradiated in phosphate buffer by 60Co γ-rays at a dose rate 19.26 Gy/min and total dose of 10 Gy in the presence of a bioreductive antitumor prodrug namely 1,4-bis [{2-(dimethylamino-N-oxide)ethyl} amino] 5, 8-dihydroxyanthracene -9,10-dione (AQ4N) and its DNA affinic reduction product 1,4-bis[{2- (dimethylamino)ethyl} amino] 5,8-dihydroxyanthracene-9,10-dione (AQ4) under air and nitrogen. AQ4N and AQ4 were found to protect against radiation-induced plasmid single and double strand breakage as assessed by agarose gel electrophoresis. The differences between the two agents, and between atmospheres of air or nitrogen were negligible. It was also found that the protection efficiencies of the compds. were pH dependent and showed maximum protection at pH 6. These results indicate that protection of DNA by AQ4 and AQ4N against radiation damage is an indirect effect since both agents are equally effective despite major differences in their DNA affinity. It is likely that radiation-induced phosphate buffer radicals are intercepted by AQ4 and AQ4N in a pH-dependent process.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 31 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:5867 HCAPLUS Full-text
DOCUMENT NUMBER: 130:231829
TITLE: Involvement of human cytochromes P450 (CYP) in the reductive metabolism of AQ4N, a hypoxia activated anthraquinone di-N-oxide prodrug
AUTHOR(S): Raleigh, S. M.; Wanogho, E.; Burke, M. Danny; McKeown, S. R.; Patterson, L. H.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, De Montfort University, Leicester, LE1 9BH, UK
SOURCE: International Journal of Radiation Oncology, Biology, Physics (1998), 42(4), 763-767
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To establish the role of the human cytochromes P 450 (CYPs) in the reductive metabolism of the novel anthraquinone di-N-oxide prodrug AQ4N. Metabolism of AQ4N was conducted in a panel of 17 human phenotyped liver microsomes. AQ4N and metabolites were detected by reverse phase isocratic HPLC. CYP inhibitors and Spearman rank correlation were used to determine the significance of AQ4N metabolism vs. specific CYP activity and/or expression. Anaerobic metabolism of AQ4N to the 2-electron reduction product, AQM, and the 4-electron reduced tertiary amine, AQ4, occurred in all 17 human liver microsome prepns. The range (± SE) for total AQ4N turnover was 14.26±1.43 nmol/incubate (highest) to 3.65±1.05 nmol/incubate (lowest). Metabolism was not detected in the absence of NADPH or microsomes. In aerobic incubates, AQM was less than 4% of anaerobic values whereas AQ4 was undetectable. CYP-mediated metabolism of AQ4N was inhibited completely by ketoconazole (KET) and carbon monoxide (CO), two global inhibitors of CYP-mediated metabolism AQ4N metabolism correlated significantly with probes for CYP 3A, specifically benzoxylresorufin O-dealkylation [r(s) = 0.70, p <0.01] and tamoxifen N-demethylation (r(s) = 0.85, p < 0.01), but not with probes for CYPs 2C, 2D, and 1A. CYP 3A involvement was confirmed by the use of the CYP 3A specific inhibitor, triacetyloleandomycin (TAO), which repressed the formation of AQM to 13% of the uninhibited value and abolished completely the formation of AQ4. Alpha-naphthoflavone (ANF), an inhibitor of CYP 2C and 1A, had no significant effect on AQ4N metabolism These data suggest that the human CYP 3A enzymes can contribute to the reductive metabolism of AQ4N. CYP 3A enzymes are highly expressed in a broad spectrum of human cancers. The results show that AQ4N requires anaerobic conditions for CYP 3A-mediated reduction and hence this subfamily of enzymes is likely to selectively activate AQ4N in hypoxic tumors .

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 32 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:723539 HCAPLUS Full-text
DOCUMENT NUMBER: 130:118930
TITLE: Reductive metabolism: its application in prodrug activation
AUTHOR(S): Patterson, Laurence H.; Raleigh, Stuart M.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, De Montfort University, Leicester, LE1 9BH, UK
SOURCE: Biomedical and Health Research (1998), 25(Drug Metabolism: Towards the Next Millennium), 72-79
CODEN: BIHREN; ISSN: 0929-6743
PUBLISHER: IOS Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 47 refs. Many disease states, including cancers have associated chronic or acute ischemic episodes resulting in tissue hypoxia. In solid tumors the poorly defined vasculature increasingly is being exploited as a way of targeting drugs to be specifically activated in hypoxic tumor regions. Drugs designed as bioreductive agents are classically based on quinone or nitroarom. structures. These include the indoloquinone derivs. (e.g. EO9), the aziridinylbenzoquinones and the nitroimidazoles (e.g. RB 6145). These agents are cytotoxic by alkylating and/or crosslinking DNA. More recently, agents based on the N-oxide functionality have been described. Specifically, tirapazamine and AQ4N appear to be most promising as bioreductively activated antitumor N-oxides although these agents have different mechanisms of action. Tirapazamine produces DNA double strand breaks consistent with its activation to a free radical. AQ4N is unique in that it is reduced to a persistent and potent inhibitor of DNA Type II topoisomerase and can kill cancer cells regardless of their oxygen status. Several NAD(P)H dependent flavoprotein enzymes including cyt P 450 reductase, xanthine oxidase, b5 reductase and DT-diaphorase are capable of reducing quinones, nitro-compds. and the heteroarom. N-oxides including tirapazamine. Cytochrome P 450 can act as a obligate 2-electron reductase in the absence of oxygen and CYP 3A subfamily is responsible for reductive bioactivation of AQ4N. This is important since CYP3A is overexpressed in many human solid cancers. Future directions for bioredn. in drug design include Antibody Directed- and Gene Directed- Enzyme Prodrug Therapy (ADEPT and GDEPT resp.). Nitro-actinomycin D, dinitrobenzamides and nitro-seco-cyclopropylindolines as prodrugs activated by bacterial aerobic nitroreductase are currently being investigated. CYP mediated activation, especially the human tumor specific CYP1B1, is also likely to figure in future bioreductive drug design.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 33 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:588296 HCAPLUS Full-text

DOCUMENT NUMBER: 129:285713

ORIGINAL REFERENCE NO.: 129:58077a,58080a

TITLE: Reduction of the indoloquinone anticancer drug EO9 by purified DT-diaphorase: a detailed kinetic study and analysis of metabolites

AUTHOR(S): Bailey, Susan M.; Lewis, Alex D.; Knox, Richard J.; Patterson, Laurence H.; Fisher, Geoff R.; Workman, Paul

CORPORATE SOURCE: CRC Beatson Laboratories, CRC Department of Medical Oncology, Glasgow, G61 1BD, UK

SOURCE: Biochemical Pharmacology (1998), 56(5), 613-621
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB DT-diaphorase (I) has been implicated in the activation and mechanism of cytotoxicity of the investigational indoloquinone anticancer drug, EO9. Here, the authors used highly purified I isolated from rat Walker tumor cells to provide unambiguous evidence for the ability of this enzyme to catalyze reduction of EO9 and to provide a more detailed characterization of the reaction. Under the conditions used, hypoxia had no effect on the initial rate of this reduction but did effect the nature and stability of metabolites formed. ESR spectroscopy showed that I reduced EO9 to a highly O2-sensitive metabolite that was probably the hydroquinone. In the presence of air, this metabolite was autoxidized to generate both drug- and O-based radicals. Comproportionation-disproportionation reactions may also be involved in the generation of these radical species. The identification of these metabolites

may contribute to the understanding of the mol. mechanism of DNA damage and cytotoxicity exerted by EO9.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 34 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:262040 HCAPLUS Full-text
DOCUMENT NUMBER: 127:60340
ORIGINAL REFERENCE NO.: 127:11357a,11360a
TITLE: DNA topoisomerase II-dependent cytotoxicity of alkylaminoanthraquinones and their N-oxides
AUTHOR(S): Smith, Paul J.; Blunt, Nicola J.; Desnoyers, Rodwige; Giles, Yvonne; Patterson, Laurence H.
CORPORATE SOURCE: College Medicine, University Wales, Cardiff, CF4 4XN, UK
SOURCE: Cancer Chemotherapy and Pharmacology (1997), 39(5), 455-461
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The role of DNA topoisomerase II (TI II) was studied in the biol. actions of a series of novel alkylaminoanthraquinones. The agents based on the anticancer TI II poison mitoxantrone, included AQ4 and AQ6, together with the corresponding mono-N-oxide (AQ6NO) and di-N-oxide (AQ4NO). The R3N+-O- modification renders the terminal nitrogen group elec. neutral and reduced AQ6NO or abolished AQ4NO-DNA binding. The inhibition of TI II decatenation activity ranked according to DNA-binding capacity. Drug-induced DNA-protein crosslinking in intact cells showed similar ranking, depending upon TI II availability. Inhibition of DNA synthesis in S-phase synchronized cultures ranked in the order of AQ6 > mitoxantrone >> AQ6NO and was independent of TI II availability. Cytotoxicity of acute 1-h exposures for all agents except the inactive AQ4NO was enhanced in a TI II-overproducing cell line.

L35 ANSWER 35 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:79693 HCAPLUS Full-text
DOCUMENT NUMBER: 126:139430
ORIGINAL REFERENCE NO.: 126:26779a,26782a
TITLE: Flow-cytometric analysis and confocal imaging of anticancer alkylaminoanthraquinones and their N-oxides in intact human cells by 647-nm krypton laser excitation
AUTHOR(S): Smith, Paul J.; Desnoyers, Rodwige; Blunt, Nicola; Giles, Yvonne; Patterson, Laurence R.; Watson, James V.
CORPORATE SOURCE: MRC Clin. Oncol. Radiother. Unit, Cambridge, UK
SOURCE: Cytometry (1997), 27(1), 43-53
CODEN: CYTODQ; ISSN: 0196-4763
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Flow cytometry and laser-scanning confocal fluorescence microscopy were used to study the pharmacodynamics, in single intact cells, of 2 novel alkylaminoanthraquinones (AQ4 and AQ6), structurally based on the mid-red-excitable but very weakly fluorescent anticancer agent mitoxantrone, and their resp. N-oxide derivs. (AQ4NO and AQ6NO). The rationale was that N-oxide modifications generate prodrug forms suitable for selective bioreductive activation in hypoxic tumor cells. DNA binding ranked in the order mitoxantrone > AQ6 > AQ4 > AQ6NO » AQ4NO. With both cytometric methods a

similar ranking was found for whole-cell and nuclear location of the compds. in human transformed fibroblasts. However, AQ6 had greater nuclear uptake than mitoxantrone, in keeping with its greater capacity to inhibit DNA synthesis. Partial charge neutralization by N-oxide derivatization resulted in loss of DNA synthesis inhibition but retention of the ability to accumulate in the cytosol, an important property for prodrug development. Thus, both flow cytometry and confocal imaging revealed biol. significant differences among the analogs with respect to subcellular distribution and retention. The study demonstrates the potential for these complementary 647-nm krypton laser line-based fluorometric methods to provide relevant structure-activity information in anthraquinone drug-design programs.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 36 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:492687 HCAPLUS Full-text
DOCUMENT NUMBER: 125:211931
ORIGINAL REFERENCE NO.: 125:39350h,39351a
TITLE: Tertiary amine N-oxides as bioreductive drugs: DACA N-oxide, nitracrine N-oxide and AQ4N
AUTHOR(S): Wilson, WR; Denny, WA; Pullen, SM; Thompson, KM; Li, AE; Patterson, LH; Lee, HH
CORPORATE SOURCE: Department Pathology, University Auckland, Auckland, N. Z.
SOURCE: British Journal of Cancer, Supplement (1996), 74(27), S43-S47
CODEN: BJCSB5; ISSN: 0306-9443
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tertiary amine N-oxides of DNA intercalators with alkylamino sidechains are a new class of bioreductive drugs. N-oxidation masks the cationic charge of the amines, forming prodrugs with low DNA binding affinity and low toxicity which can be activated selectively by metabolic reduction under hypoxic conditions. This study compares three intercalator N-oxides (NC-NO, DACA-NO and AQ4N), which, resp., give nitracrine (NC), DACA and AQ4 on reduction In aerobic cell culture all three N-oxides were much less toxic than the corresponding amines, and showed large increases in cytotoxicity under hypoxia. The topoisomerase poisons DACA and AQ4 (and their N-oxides) were less active against non-cycling than cycling cells. However, only AQ4N was active against the mouse mammary tumor MDAH-MCa-4. This dialkylaminoanthraquinone-di-N-oxide has activity at least as great as the reference bioreductive drug RB 6145 against this tumor, both with and without radiation and when combined with the tumor blood flow inhibitor 5,6-dimethylxanthenone-4- acetic acid (DMXAA). It is suggested that the high in vivo activity of AQ4N relative to the other topoisomerase-targeted N-oxide, DACA-NO, may be in part due to release in hypoxic cells of an intracalator with sufficiently high DNA binding affinity that it is retained long enough to kill non-cycling cells when they eventually re-enter the cell cycle.

L35 ANSWER 37 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:492686 HCAPLUS Full-text
DOCUMENT NUMBER: 125:189538
ORIGINAL REFERENCE NO.: 125:35367a,35370a
TITLE: Evidence for a therapeutic gain when AQ4N or tirapazamine is combined with radiation
AUTHOR(S): McKeown, S. R.; Friery, O. P.; McIntyre, I. A.; Hejmadi, M. V.; Patterson, L. H.; Hirst, D. G.

CORPORATE SOURCE: School Biomedical Sciences, University Ulster, Jordanstown, BT37 0QB, UK
SOURCE: British Journal of Cancer, Supplement (1996), 74(27), S39-S42
CODEN: BJCSB5; ISSN: 0306-9443
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The use of bioreductive drugs as an adjunct to radiotherapy in the treatment of cancer is presently being tested in several clin. trials worldwide. We have developed a novel bioreductive compound AQ4N (1,4-bis-{[2-(dimethylamino-N-oxide)ethyl]amino}5,8-dihydroxy- anthracene-9,10-dione) which can be reduced to a stable cytotoxic agent AQ4. The anti-tumor efficacy of AQ4N has been studied using male BDF mice bearing the T50/80 tumor. AQ4N in combination with single dose x-irradiation (12 Gy) and also with two fractionated radiation regimens was examined (5 + 3 Gy, one fraction per day; or 10 + 2 Gy fractions, 2 fractions per day with an 8 h interval). Results show that in all combinations tested there was a marked increase in anti-tumor efficacy. This was also found in the single dose regimen for the bioreductive drug tirapazamine (SR 4233; 3-amino-1,2,4-benzotriazine-1,4-dioxide). Normal tissue toxicity of drug-radiation combinations was measured by assessing function in the eccrine sweat gland of the mouse hind foot. When combined with 10 Gy radiation neither AQ4N nor tirapazamine showed any enhancement of functional loss as compared with radiation alone. This was in contrast to mitomycin C which had a marked effect on the radiation induced functional deficit. In conclusion, in our model, an increase in the therapeutic index was obtained for radiation treatment when either AQ4N or tirapazamine was administered concurrently.

L35 ANSWER 38 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:166048 HCAPLUS Full-text
DOCUMENT NUMBER: 124:278232
ORIGINAL REFERENCE NO.: 124:51163a
TITLE: DNA damage following combination of radiation with the bioreductive drug AQ4N: Possible selective toxicity to oxic and hypoxic tumor cells
AUTHOR(S): Hejmadi, M. V.; McKeown, S. R.; Friery, O. P.; McIntyre, I. A.; Patterson, LH; Hirst, DG
CORPORATE SOURCE: School Biomedical Sciences, University Ulster, Jordanstown, BT37 0QB, Ire.
SOURCE: British Journal of Cancer (1996), 73(4), 499-505
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB AQ4N (1,4-bis-{[2-(dimethylamino-N-oxide)ethyl]amino}5,8- dihydroxyanthracene-9,10-dione) is a novel bioreductive agent that can be reduced to a stable, DNA-affinic compound, AQ4. The alkaline comet assay was used to evaluate DNA damage induced by AQ4N and radiation. Cells prepared from freshly excised T50/80 murine tumors were shown to have the ability to reduce AQ4N to a DNA-damaging agent; this had disappeared within 24 h of excision. When T50/80 tumors implanted in BDF mice were exposed to radiation in vivo a considerable amount of DNA damage was present in tumors excised immediately. Minimal levels of DNA damage were detectable in tumors excised after 2-5 h. AQ4N given 30 min before radiation had no appreciable influence on this effect and AQ4N alone caused only a small amount of damage. When AQ4N and radiation were combined an increasing number of damaged cells were seen in tumors excised 24-96 h after irradiation This was interpreted as evidence of the continued presence of AQ4, or AQ4-induced damage, which was formed in cells hypoxic at

the time of administration of AQ4N. AQ4, a potent topoisomerase II inhibitor, would be capable of damaging cells recruited into the cell cycle following radiation damage to the well-oxygenated cells of the tumor. The kinetics of the expression of the DNA damage is consistent with this hypothesis and shows that AQ4 has persistent activity in vivo.

L35 ANSWER 39 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:120741 HCAPLUS Full-text
DOCUMENT NUMBER: 124:168998
ORIGINAL REFERENCE NO.: 124:31211a,31214a
TITLE: Rationalization of the C-S lyase activity of aspartate aminotransferase
AUTHOR(S): Teesdale-Spittle, Paul H.; Adcock, Harriet J.; Patterson, Laurence H.; Buckberry, Lorraine D.
CORPORATE SOURCE: Sch. of Applied Sciences, De Montfort Univ., Leicester, LE1 9BH, UK
SOURCE: Biochemical Society Transactions (1996), 24(1), 141S
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The structure-activity profile of aspartate aminotransferase was rationalized for C-S lyase activity on the basis of Van der Waals overlap between the cysteine conjugate and the enzyme active site and ease of elimination of the thiolate RS'. Mol. modeling data were obtained for the interactions between dibromophenyl, chlorodifluoroethyl, benzthiazolyl, and trichlorovinyl cysteine conjugates and the aspartate aminotransferase active site.

L35 ANSWER 40 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:798132 HCAPLUS Full-text
DOCUMENT NUMBER: 123:275331
ORIGINAL REFERENCE NO.: 123:48939a,48942a
TITLE: AQ4N: An alkylaminoanthraquinone N-oxide showing bioreductive potential and positive interaction with radiation in vivo
AUTHOR(S): McKeown, S R.; Hejmadi, M V.; McIntyre, I A.; McAleer, J J A.; Patterson, L H.
CORPORATE SOURCE: School Biomedical Sciences, University Ulster, BT37 0QB, UK
SOURCE: British Journal of Cancer (1995), 72(1), 76-81
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Macmillan Scientific & Medical Division
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AQ4N (1,4-bis-{[2-(dimethylamino-N-oxide)ethyl]amino}5,8-dihydroxy-anthracene-9,10-dione) is a novel alkylaminoanthraquinone N-oxide which, on reduction, forms a stable DNA affinic cytotoxic compound AQ4. The in vivo anti-tumor efficacy of AQ4N was investigated in B6D2F1 mice bearing the T50/80 mammary carcinoma. The effect of the drug was evaluated in combination with hypobaric hypoxia and with radiation (single and multiple fractions). Systemic toxicity was assessed by weight loss post treatment. This was low for AQ4N and was less than that obtained with the bioreductive drugs, RSU 1069 (1-[3-aziridinyl-2- hydroxypropyl]-2-nitroimidazole) and SR 4233 (Tirapazamine, 3-amino-1,2,4-benzotriazine-1,4-dioxide). The anti-tumor effect of AQ4N was potentiated in vivo by combination with hypobaric hypoxia with a dose enhancement ratio of 5.1. This is consistent with the proposal that AQ4N was reduced in vivo to AQ4, resulting in enhanced anti- tumor

toxicity. When AQ4N (200 mg kg-1) was combined with single dose radiation (12 Gy) the drug was shown to have an additive interaction with radiation. This was obtained even if the drug was administered from 4 days before to 6 h after radiation treatment. Equivalent anti- tumor activity was also shown when both AQ4N (200 mg kg-1) and radiation (5 + 3 Gy) were administered in fractionated schedules. In conclusion, AQ4N shows significant potential as a bioreductive drug for combination with fractionated radiotherapy.

L35 ANSWER 41 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:523488 HCAPLUS Full-text
DOCUMENT NUMBER: 122:281401
ORIGINAL REFERENCE NO.: 122:51015a,51018a
TITLE: Aliphatic amine N-oxides of DNA binding agents as bioreductive drugs
AUTHOR(S): Patterson, Laurence H.; Craven, Michael R.; Fisher, Geoffrey R.; Teesdale-Spittle, Paul
CORPORATE SOURCE: School of Applied Sciences, De Montfort University, Leicester, LE1 9BH, UK
SOURCE: Oncology Research (1994), 6(10-11), 533-8
CODEN: ONREE8; ISSN: 0965-0407
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The DNA binding and cytotoxicity of four intercalating agents, namely bis-alkylamino (-N(CH2)2N(CH3)2) substituted anthraquinone, anthrapyrazole and anthracene, and mono (N(CH2)2N(CH3)2) acridinone, have been compared with their resp. aliphatic amine N-oxides -N(CH2)2N+(O-)(CH3)2. The results show that, unlike the intercalators, the N-oxides do not bind to DNA. Mol. modeling illustrates that the δ+ nature of the intercalator alkylamino side chains in the protonated form allows for an attractive electrostatic interaction with phosphates of the DNA backbone, whereas the δ- partial charge on the N-oxide makes such an interaction not permissible; indeed, the electrostatic interaction with the DNA phosphates will be repulsive. The N-oxides show little or no cytotoxicity against V79 cells at concns. equimolar to the IC90 (concentration that inhibits 90% of cell proliferation) of the resp. intercalators. However, the cytotoxicity of anthrapyrazole N-oxide against hypoxic V79 cells in the presence of an activating system of S9 liver fraction was enhanced significantly. The results indicate that N-oxides of DNA-affinic agents have potential as bioreductive prodrugs, since they possess low aerobic toxicity but under hypoxic conditions can be metabolized to a potent cytotoxic species presumed to be a DNA-binding tertiary amine.

L35 ANSWER 42 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:45334 HCAPLUS Full-text
DOCUMENT NUMBER: 120:45334
ORIGINAL REFERENCE NO.: 120:8079a,8082a
TITLE: A comparison of free radical formation by quinone antitumor agents in MCF-7 cells and the role of NAD(P)H (quinone -acceptor) oxidoreductase (DT-diaphorase)
AUTHOR(S): Fisher, Geoffrey R.; Patterson, Laurence H.; Gutierrez, Peter L.
CORPORATE SOURCE: Dep. Biol. Chem., Univ. Maryland Cancer Cent., Baltimore, MD, 21201, USA
SOURCE: Chemico-Biological Interactions (1993), 88(2-3), 137-53
CODEN: CBINA8; ISSN: 0009-2797
DOCUMENT TYPE: Journal

LANGUAGE: English

AB EPR/ESR spin trapping studies with DMPO revealed that purified rat liver NAD(P)H (quinone-acceptor) oxidoreductase (QAO) mediated hydroxyl radical formation by a diverse range of quinone-based antitumor agents. However, when MCF-7 S9 cell fraction was the source of QAO, EPR studies distinguished four different interactions by these agents and QAO with respect to hydroxyl radical formation: (i) hydroxyl radical formation by diaziquone (AZQ), menadione, 1AQ (I); 1,5AQ (II)and 1,8AQ (III) was mediated entirely or partially by QAO in MCF-7 S9 fraction; (ii) hydroxyl radical formation by daunorubicin and Adriamycin was not mediated by QAO in MCF-7 S9 fraction; (iii) hydroxyl radical formation by mitomycin C was stimulated in MCF-7 S9 fraction when QAO was inhibited by dicumarol; (i.v.) no hydroxyl radical formation was detected for 1,4AQ (IV) or mitoxantrone in MCF-7 S9 fraction. This study shows that purified rat liver QAO can mediate hydroxyl radical formation by a variety of diverse quinone antitumor agents. However, QAO did not necessarily contribute to hydroxyl radical formation by these agents in MCF-7 S9 fraction and in the case of mitomycin C, QAO played a protective role against hydroxyl radical formation.

L35 ANSWER 43 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:22888 HCAPLUS Full-text

DOCUMENT NUMBER: 120:22888

ORIGINAL REFERENCE NO.: 120:4105a,4108a

TITLE: Rationale for the use of aliphatic N-oxides of cytotoxic anthraquinones as prodrug DNA binding agents: a new class of bioreductive agent

AUTHOR(S): Patterson, Laurence H.

CORPORATE SOURCE: Sch. App. Sci., De Montfort Univ., The Gateway/Leicester, LE1 9BH, UK

SOURCE: Cancer and Metastasis Reviews (1993), 12(2), 119-34
CODEN: CMRED4; ISSN: 0167-7659

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 91 refs. NAD(P)H dependent cytochrome P 450's and other hemoproteins under hypoxia, mediate two-electron reduction of a wide range of structurally dissimilar N-oxides to their resp. tertiary amines. Metabolic reduction can be utilized, in acute and chronic hypoxia, to convert N-oxides of DNA affinic agents to potent and persistent cytotoxins. In this respect a knowledge of N-oxide bioredn. and the importance of the cationic nature of agents that bind to DNA by intercalation can be combined to rationalize N-oxides as pro-drugs of DNA binding agents. The concept is illustrated using the alkylaminoanthraquinones which are a group of cytotoxic agents with DNA binding affinity that is dependent on the cationic nature of these compds. The actions of the alkylaminoanthraquinones involve drug intercalation into DNA (and double stranded RNA) and inhibition of both DNA and RNA polymerases and topoisomerase Type I and II. A di-N-oxide analog of mitoxantrone, 1,4-bis{[2-(dimethylamino-N-oxide)ethyl]amino}5,8- dihydroxyanthracene-9,10-dione (AQ4N) has been shown to possess no intrinsic binding affinity for DNA and has low toxicity. Yet in the absence of air AQ4N can be reduced in vitro to a DNA affinic agent with up to 1000-fold increase in cytotoxic potency. Importantly the reduction product, AQ4, is stable under oxic conditions. Studies in vivo indicate that antitumor activity of AQ4N is manifest under conditions that promote transient hypoxia and/or diminish the oxic tumor fraction. The advantage of utilizing the reductive environment of hypoxic tumors to reduce N-oxides is that, unlike conventional bioreductive agents, the resulting products will remain active even if the hypoxia that led to bioactivation is transient or the active compds., once formed, diffuse away from the hypoxic tumor regions. Furthermore, the DNA affinic nature of the active compds. should ensure their localization in tumor tissue.

L35 ANSWER 44 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:213065 HCAPLUS Full-text
DOCUMENT NUMBER: 118:213065
ORIGINAL REFERENCE NO.: 118:36731a,36734a
TITLE: Preparation of anticancer anthrapyrazole compounds
INVENTOR(S): Patterson, Laurence Hylton
PATENT ASSIGNEE(S): British Technology Group Ltd., UK
SOURCE: Brit. UK Pat. Appl., 23 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2254614	A	19921014	GB 1992-7958	19920410
GB 2254614	B	19950201		
CA 2108255	A1	19921013	CA 1992-2108255	19920410
WO 9218485	A1	19921029	WO 1992-GB645	19920410
W: AU, CA, FI, HU, JP, KR, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9215375	A	19921117	AU 1992-15375	19920410
AU 662278	B2	19950824		
EP 579647	A1	19940126	EP 1992-907671	19920410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06506457	T	19940721	JP 1992-507712	19920410
US 5447950	A	19950905	US 1993-133034	19931022
PRIORITY APPLN. INFO.:			GB 1991-7852 A	19910412
			WO 1992-GB645 A	19920410

OTHER SOURCE(S): MARPAT 118:213065
AB Title compds. I [R1 = AN(O)R'R'' and R2-R4 = H, X, NHAN(O)R'R'' wherein X = HO, halo, H2N, C1-4 alkoxy, C2-8 alkanoyloxy; A = C2-4 alkylene with a chain length between N or NH and NOR'R'' of at least 2 C atoms; R', R'' = C1-4 alkyl, C2-4 hydroxyalkyl, C3-4 dihydroxyalkyl such that the C attached to N does not carry a HO group and no C is substituted by 2 HO groups; or R'R'' = alkylene] and salts, useful as anticancer prodrugs (no data), are prepared Thus, I (R1 = Me2NCH2CH2, R2 = 5-Me2NCH2CH2NH, R3 = R4 = H) (preparation given) in CH2Cl2 was treated with 3-ClC6H4C(O)OOH at 0° to give I [R1 = Me2N(O)CH2CH2, R2 = 5-Me2N(O)CH2CH2NH, R3 = R4 = H].

L35 ANSWER 45 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:147332 HCAPLUS Full-text
DOCUMENT NUMBER: 118:147332
ORIGINAL REFERENCE NO.: 118:25327a,25330a
TITLE: Anti-cancer anthracene amine N-oxide prodrugs and their preparation
INVENTOR(S): Patterson, Laurence Hylton
PATENT ASSIGNEE(S): British Technology Group Ltd., UK
SOURCE: Brit. UK Pat. Appl., 19 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2254613	A	19921014	GB 1992-7957	19920410
GB 2254613	B	19950125		
CA 2108256	A1	19921013	CA 1992-2108256	19920410
WO 9218469	A1	19921029	WO 1992-GB646	19920410
W: AU, CA, FI, HU, JP, KR, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9215376	A	19921117	AU 1992-15376	19920410
AU 660883	B2	19950706		
ZA 9202641	A	19931011	ZA 1992-2641	19920410
EP 579646	A1	19940126	EP 1992-907670	19920410
EP 579646	B1	19951227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06506923	T	19940804	JP 1992-507713	19920410
AT 132136	T	19960115	AT 1992-907670	19920410
ES 2082461	T3	19960316	ES 1992-907670	19920410
US 5461078	A	19951024	US 1993-133033	19931012

PRIORITY APPLN. INFO.: GB 1991-7843 A 19910412
WO 1992-GB646 A 19920410

OTHER SOURCE(S): MARPAT 118:147332

AB Title N-oxides I [R1 = various sidechains containing an N-oxide of a tertiary or (hetero)cyclic amine; R2 = H, or as given for R1; R3-R6 = H, OH, halo, amino, C1-4 alkoxy, C2-8 alkanoyloxy] and salts are claimed, useful as prodrugs, with low cytotoxicity because they are bioreduced within anaerobic neoplastic tissue to the active amine anticancer agents (no data). I are also potentially useful against anaerobic bacterial and protozoal infections. For example, neat reaction of 9,10-bis(chloromethyl)anthracene with Me2NCH2CH2NH2 at reflux, N-oxidation of the resulting bis[[(dimethylamino)ethyl]aminomethyl] compound with 3-ClC6H4C(O)OOH in CH2Cl2, and chromatog on silica gel, gave I [R1 = R2 = CH2NHCH2CH2N(O)Me2; R3-R6 = H].

L35 ANSWER 46 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:257 HCAPLUS Full-text
DOCUMENT NUMBER: 118:257
ORIGINAL REFERENCE NO.: 118:46h,47a
TITLE: Lack of involvement of reactive oxygen in the cytotoxicity of mitoxantrone, CI941 and ametantrone in MCF-7 cells: comparison with doxorubicin
AUTHOR(S): Fisher, Geoffrey R.; Patterson, Laurence H.
CORPORATE SOURCE: Dep. Pharm., Leicester Polytech., Leicester, LE1 9BH, UK
SOURCE: Cancer Chemotherapy and Pharmacology (1992), 30(6), 451-8
CODEN: CCPHDZ; ISSN: 0344-5704
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The MCF-7 cell S9 fraction and whole MCF-7 cells can mediate one-electron-redox cycling of doxorubicin, giving rise to concomitant oxidation of reduced NADP (NADPH), formation of superoxide anions and hydroxyl radicals. Doxorubicin redox cycling was consistent with DNA strand breakage and cell kill in MCF-7 cells. In contrast, no evidence for redox cycling was found for mixtoxantrone (MIT), CI941 or ametantrone (AMET) in MCF-7 cells. Despite the absence of redox cycling, the CI941, MIT, and AMET concns. resulting in 50% mortality (LC50; 1.5 x 10-10, 5.2 x 10-9 and 1.2 x 10-6 M, resp.) of MCF-7 cells were lower than that of DOX (3.0 x 10-6 M). Furthermore, the higher cytotoxicity of MIT and CI941 as compared with AMET or DOX was associated with greater efficiency in inducing DNA strand breakage in MCF-7 cells as determined by alkaline elution. Since MIT and CI941 proved to be the most

potent DNA-damaging and cytotoxic agents in this study, the ability of DOX to undergo redox cycling does not appear to confer increased cytotoxic potential on this agent. The present study revealed several important aspects with regards to the structural modification of anthraquinone antitumor agents. Firstly, the C1 and C4 postitioning of the hydroxyethylamino side chains on MIT, CI941 and AMET is associated with a lack of flavin reductase-mediated activation of these agents. Secondly, the possession of a C5 or C8 aromatic hydroxyl group appears to be intimately involved in the enhanced DNA strand breakage and cytotoxic potency of MIT and CI941, since AMET does not possess these groups. These findings indicate that future development of quinone antitumor agents should concentrate on compds. that do not undergo redox cycling but do possess aromatic hydroxyl groups, since the latter appear to be responsible for the enhanced cytotoxicity of MIT and CI941.

L35 ANSWER 47 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:165893 HCAPLUS Full-text
DOCUMENT NUMBER: 116:165893
ORIGINAL REFERENCE NO.: 116:27807a,27810a
TITLE: NAD(P)H (quinone acceptor) oxidoreductase (DT-diaphorase)-mediated two-electron reduction of anthraquinone-based antitumor agents and generation of hydroxyl radicals
AUTHOR(S): Fisher, Geoffrey R.; Gutierrez, Peter L.; Oldcorne, Mark A.; Patterson, Laurence H.
CORPORATE SOURCE: Dep. Pharm., Leicester Polytech., Leicester, LE1 9BH, UK
SOURCE: Biochemical Pharmacology (1992), 43(3), 575-85
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The anthraquinone-based antitumor agents mitoxantrone, daunorubicin and ametantrone were found to be substrates for NAD(P)H (quinone acceptor) oxidoreductase (DT-diaphorase) [QAO] isolated from rat liver. This was indicated by the stimulation of QAO-dependent NADPH oxidation by these agents. This effect followed Michaelis-Menten kinetics and was dependent on the concentration of QAO, inhibited by the specific QAO inhibitor dicumarol (15 μM) and enhanced by the QAO activators bovine serum albumin (0.01%) and Triton X-100 (0.03%). As indicated by the Vmax/Km ratio, mitoxantrone (26.53) was considerably more active than ametantrone (11.25) or daunorubicin (7.35). Metabolism of these anthraquinones was associated with the formation of superoxide anions, hydrogen peroxide and hydroxyl radicals as indicated by ESR spin trapping studies with 5,5-dimethyl-1-pyrroline-N-oxide. This is likely to be due to the slow auto-oxidation of the resp. dehydroquinones in the presence of mol. oxygen. QAO needs to be considered as a possible route of bioreductive activation of these agents.

L35 ANSWER 48 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:582880 HCAPLUS Full-text
DOCUMENT NUMBER: 115:182880
ORIGINAL REFERENCE NO.: 115:31217a,31220a
TITLE: Preparation of [(dialkylamino)alkylamino] anthraquinone dioxides as neoplasm inhibitors
INVENTOR(S): Patterson, Laurence Hylton
PATENT ASSIGNEE(S): National Research Development Corp., UK
SOURCE: Brit. UK Pat. Appl., 34 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2237283	A	19910501	GB 1990-22217	19901012
GB 2237283	B	19930127		
CA 2038934	A1	19910414	CA 1990-2038934	19901012
CA 2038934	C	20021119		
WO 9105824	A1	19910502	WO 1990-GB1574	19901012
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9065395	A	19910516	AU 1990-65395	19901012
AU 634125	B2	19930211		
EP 450021	A1	19911009	EP 1990-915322	19901012
EP 450021	B1	19940202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 04502166	T	19920416	JP 1990-514278	19901012
JP 2854971	B2	19990210		
ZA 9008178	A	19920624	ZA 1990-8178	19901012
AT 101181	T	19940215	AT 1990-915322	19901012
ES 2062558	T3	19941216	ES 1990-915322	19901012
US 5132327	A	19920721	US 1991-674354	19910410

PRIORITY APPLN. INFO.: GB 1989-23075 A 19891013
EP 1990-915322 A 19901012
WO 1990-GB1574 A 19901012

OTHER SOURCE(S): MARPAT 115:182880

AB Title compds. I [R1-R4 = H, X, NHANHR, NHAN(O)R5R6; X = OH, halo, NH2, C1-4 alkoxy, C2-8 alkanoxyloxy; A = C2-4 alkylene; R,R5,R6 = C1-4 alkyl, C2-4 hydroxyalkyl, C2-4 dihydroxyalkyl, or NR5R6 = 3-7 membered heterocyclyl; at least one of R1-R4 = NHAN(O)R5R6, other provisos given], were prepared Thus, a solution of 1,5-dichloroanthracene-9,10-dione in 2-(diethylamino)ethylamine was refluxed 4 h and the resulting product was oxidized by MCPBA to give title compound II. II was active against MCF-7 human breast cancer cells under aerobic and anaerobic conditions.

L35 ANSWER 49 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:400328 HCAPLUS Full-text
DOCUMENT NUMBER: 115:328
ORIGINAL REFERENCE NO.: 115:59a,62a
TITLE: Involvement of hydroxyl radical formation and DNA strand breakage in the cytotoxicity of anthraquinone antitumor agents
AUTHOR(S): Fisher, G. R.; Brown, J. R.; Patterson, L. H.
CORPORATE SOURCE: Dep. Pharm., Leicester Polytech., Leicester, LE1 9BH, UK
SOURCE: Free Radical Research Communications (1990), 11(1-3), 117-25
CODEN: FRRCEX; ISSN: 8755-0199
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Four 9,10-anthraquinones (AQ) group were studied. 1-AQ (I, R1 = R2 = R3 = H), 1,5-AQ, I [R1 = R3 = H; R2 = NH(CH2)2NH(CH2)2OH], and 1,8-AQ, I [R1 = R2 = H; R3 = NH(CH2)2NH(CH2)2OH], but not 1,4-AQ, I [R1 = NH(CH2)2NH(CH2)2OH; R2 = R3 = H], (100 μM) generated pBR322 plasmid DNA single strand breaks in the presence of purified NADPH dependent cytochrome P 450 reductase. 1-AQ, 1,5-AQ and 1,8-AQ (at 100 μM) stimulated hydroxyl radical formation in MCF-7 S9 cell fraction (as measured by dimethylpyrroline N-oxide spin trapping) and MCF-7

DNA strand breaks as measured by alkaline filter elution. In contrast, 1,4-AQ did not stimulate hydroxyl radical formation and produced considerably less strand breaks in MCF-7 cells compared to the other AQ's. It would appear that the position of the -NH(CH2)2NH(CH2)2OH groups on the chromophore is an important determinant in the metabolic activation of cytotoxic anthraquinones. This may contribute to the cytotoxicity (ID50 values) of 1-AQ (0.06 μM), 1-8-AQ (0.5 μM) and 1,5-AQ (12.3 μM) but not the 1,4-AQ (1.2 μM).

L35 ANSWER 50 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:135697 HCAPLUS Full-text
DOCUMENT NUMBER: 114:135697
ORIGINAL REFERENCE NO.: 114:22837a,22840a
TITLE: DNA strand breakage by peroxidase-activated mitoxantrone
AUTHOR(S): Fisher, Geoffrey R.; Patterson, Laurence H.
CORPORATE SOURCE: Dep. Pharm., Leicester Polytech., Leicester, LE1 9BH, UK
SOURCE: Journal of Pharmacy and Pharmacology (1991), 43(1), 65-8
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Spectroscopic evidence demonstrates that the alkylaminoanthraquinone mitoxantrone is a substrate for horseradish peroxidase in the presence of hydrogen peroxide and that the result of this interaction is the formation of an air-stable mitoxantrone-derived free radical. The mitoxantrone-derived free radicals or their further oxidation products appear to extensively cross-link with plasmid DNA by a reaction that is mitoxantrone concentration-dependent. Oxidative activation of mitoxantrone to a DNA-damaging species may contribute to the mechanism of action of this antitumor agent.

L35 ANSWER 51 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:91332 HCAPLUS Full-text
DOCUMENT NUMBER: 112:91332
ORIGINAL REFERENCE NO.: 112:15319a,15322a
TITLE: Redox cycling in MCF-7 human breast cancer cells by antitumor agents based on mitozantrone
AUTHOR(S): Fisher, G. R.; Brown, J. R.; Patterson, L. H.
CORPORATE SOURCE: Dep. Pharm., Leicester Polytech., Leicester, LE1 9BH, UK
SOURCE: Free Radical Research Communications (1989), 7(3-6), 221-6
CODEN: FRRCEX; ISSN: 8755-0199
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a series of (hydroxyethylaminoalkylamino)anthraquinones (AQ's) (I; R1 = H, NH(Me)2NHEtOH, R2 = R3 = OH, H, NH(Me)2NHEtOH) based on mitoxantrone, 1-AQ and 1,8-AQ stimulated basal rate NADPH oxidation whereas 1,4-AQ, 1,5-AQ and mitoxantrone had no effect. A similar trend was observed for superoxide generation by these compds. in MCF-7 S9 protein fraction: 1-AQ and 1,8-AQ were active, whereas 1,5-AQ, 1,4-AQ and mitoxantrone had no effect. All the AQ's including mitoxantrone were cytotoxic to MCF-7 cells in a concentration-dependent manner with EC50 values as follows: 1-AQ (0.01 μM), doxorubicin (0.4 μM), mitoxantrone (0.6 μM), 1,8-AQ (2.0 μM), 1,5-AQ (4.0 μM), and 1,4-AQ (8.0 μM). Thus the redox-active AQ's were also the most cytotoxic. Mitoxantrone was not redox active but was more cytotoxic than all but 1-AQ, hence factors

other than free radical generation contribute to the antitumor activity of this group of compds.

L35 ANSWER 52 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:586902 HCAPLUS Full-text
DOCUMENT NUMBER: 111:186902
ORIGINAL REFERENCE NO.: 111:30859a,30862a
TITLE: Free radical formation by cytotoxic alkylaminoanthraquinones in liver microsomes
AUTHOR(S): Patterson, Laurence H.; Basra, Jaspal; Brown, Jeffrey R.
CORPORATE SOURCE: Sch. Pharm., Leicester Polytech., Leicester, LE1 9BH, UK
SOURCE: Basic Life Sciences (1988), 49(Oxygen Radicals Biol. Med.), 803-6
CODEN: BLFSBY; ISSN: 0090-5542
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of radicals from 4 alkylaminoanthraquinones [I, R1, R2, R3 = H or NH(CH2)2NEt2] was studied in mouse liver microsome prepns. by ESR. In the absence of oxygen steady state levels of the radical species were formed with the participation of NADPH. In the presence of oxygen these radicals generated superoxide radicals and apparently served as carriers of electrons form NADPH to superoxide. Since this radical mechanism is analogous to that of doxorubicin, it may be involved in the cytotoxicity of these compds. The position of substituents in I influenced the reaction rates.

L35 ANSWER 53 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:31471 HCAPLUS Full-text
DOCUMENT NUMBER: 108:31471
ORIGINAL REFERENCE NO.: 108:5129a,5132a
TITLE: The effect of the anthrapyrazole antitumor agent CI941 on rat liver microsome- and cytochrome P-450 reductase-mediated free-radical processes. Inhibition of doxorubicin activation in vitro
AUTHOR(S): Graham, Martin A.; Newell, David R.; Butler, John; Hoey, Brigid; Patterson, Laurence H.
CORPORATE SOURCE: Drug Dev. Sect., Inst. Cancer Res., Sutton/Surrey, SM2 5PX, UK
SOURCE: Biochemical Pharmacology (1987), 36(20), 3345-51
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pulse radiolysis of CI941 (I) demonstrated that the drug can undergo chemical reduction, with a 1-electron reduction potential of E1/7 = -538 mV. However, ESR spectroscopy studies with either NADPH-fortified microsomes or cytochrome P 450 reductase from rats failed to detect a drug free radical signal. Unlike doxorubicin, CI941 (150 μM) inhibited basal microsomal NADPH consumption by 45%. Furthermore, CI941 (50-200 μM) antagonized doxorubicin-stimulated NADPH oxidation by >50%. CI941 also antagonized the formation of a doxorubicin free radical ESR signal in a concentration-dependent manner. CI941 induced minimal superoxide generation in the presence of either microsomes or cytochrome P 450 reductase and inhibited doxorubicin-induced (50 μM) superoxide formation by ≤80%. Importantly, CI941 inhibited both basal and doxorubicin (100 μM)-stimulated lipid peroxidn. (52% inhibition at 5 μM CI941). Apparently, CI941 is unlikely to induce free radical-mediated tissue damage in vivo. On the

contrary, CI941 may have a protective role if used in combination with doxorubicin.

L35 ANSWER 54 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1985:400185 HCAPLUS Full-text
DOCUMENT NUMBER: 103:185
ORIGINAL REFERENCE NO.: 103:31a,34a
TITLE: Comparative computer graphics and solution studies of the DNA interaction of substituted anthraquinones based on doxorubicin and mitoxantrone
AUTHOR(S): Islam, Suhail A.; Neidle, Stephen; Gandecha, Bijukumar M.; Partridge, Malcolm; Patterson, Laurence H. ; Brown, Jeffrey R.
CORPORATE SOURCE: Dep. Biophys., King's Coll., London, WC2B 5RL, UK
SOURCE: Journal of Medicinal Chemistry (1985), 28(7), 857-64
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The title anthraquinones I (R1 = R2 = H or NHCH2CH2NEt2; R3 = H) prepared by the reaction of the appropriate anthraquinone with 2-(diethylamino)ethylamine [100-36-7], and 1,8-bis[[2- (diethylamino)ethyl]amino]anthracene-9,10-diione (I; R1 and R2 = H; R3 = NHCH2CH2NEt2)(II) [75312-57-1] were shown to intercalate with DNA. The results from solution studies of the DNA binding of I and II were correlated with the results from computer graphics modeling of their fit into a DNA-intercalation site. I and II showed bathochromic and hypochromic shifts, with an isosbestic point in the visible region of the spectrum, on binding to DNA. All compds. using ccc-DNA and the degree of unwinding/drug mol. was 10.6 and 14.2-14.3° for mono- and disubstituted compds., resp. I and II as their HCl salts evaluated against P-388 leukemia in mice, and for antiproliferative effect against HeLa and Hep2 cell lines, showed no activity against leukemia but have an antiproliferative effect on the above cell lines.

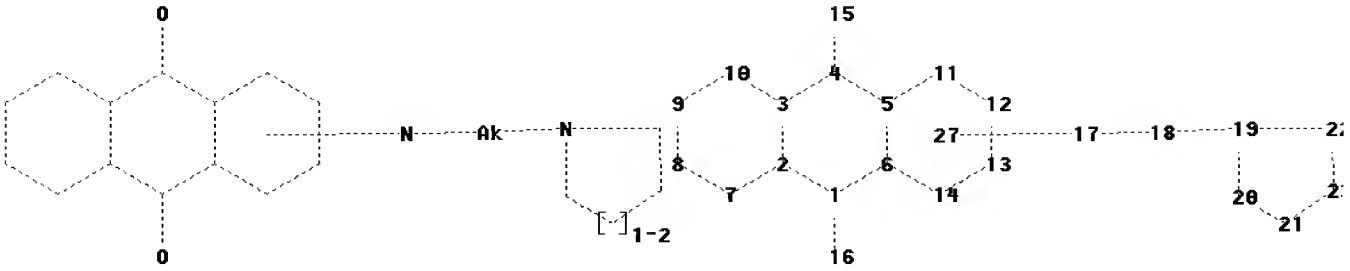
L35 ANSWER 55 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:546237 HCAPLUS Full-text
DOCUMENT NUMBER: 101:146237
ORIGINAL REFERENCE NO.: 101:22077a,22080a
TITLE: Anthraquinone free-radical formation by mouse liver subcellular fractions
AUTHOR(S): Oldcorne, Mark A.; Brown, Jeffrey R.; Patterson, Laurence H.
CORPORATE SOURCE: Sch. Pharm., Leicester Polytech., Leicester, LE1 9BH, UK
SOURCE: Biochemical Society Transactions (1984), 12(4), 681-2
CODEN: BCSTB5; ISSN: 0300-5127
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mouse liver microsome, nuclei, and cytosol prepns. reduced 1,4-dihydroxyanthraquinone to a free radical as monitored by ESR spectroscopy. Exogenous NADPH was required for free radical formation by microsomes and nuclei, but not for that by cytosol prepns. (presumably due to the presence of endogenous reducing equivs.). Microsomes also formed a free radical on incubation with anthraquinone; however, the signal intensity was 6.5-fold lower than that for the dihydroxy derivative Observation of the free radical signals demonstrated a strict requirement for anaerobic conditions.

L35 ANSWER 56 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1983:498884 HCAPLUS Full-text
DOCUMENT NUMBER: 99:98884
ORIGINAL REFERENCE NO.: 99:15093a,15096a
TITLE: Computer graphics in rational anticancer drug design
AUTHOR(S): Islam, S. A.; Kuroda, R.; Neidle, S.; Brown, J. R.; Gandecha, B. M.; Patterson, L. H.
CORPORATE SOURCE: Dep. Biophys., King's Coll., London, WC2B 5RL, UK
SOURCE: Biochemical Society Transactions (1982), 10(6), 501
CODEN: BCSTB5; ISSN: 0300-5127
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Computer graphics were used to simulate the docking of 1-, 1,4-, 1,5-, and 1,8-substituted anthraquinones (I; R1-R3 = NHCH2CH2NEt2) into the double helical deoxy(CpG) fragment intercalation site; all of these mols. have geometries defined by x-ray-crystallog. analyses. There were marked differences between the anthraquinones in the low-energy stable orientation. The extents of interaction of the various compds. were quant. detd; this permitted a definition of the mol. features responsible for optimal binding.

L35 ANSWER 57 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1983:119275 HCAPLUS Full-text
DOCUMENT NUMBER: 98:119275
ORIGINAL REFERENCE NO.: 98:18005a,18008a
TITLE: 1,4-Bis{2-[(2-hydroxyethyl)amino]ethylamino}-9,10-anthracenedione, an anthraquinone antitumor agent that does not cause lipid peroxidation in vivo; comparison with daunorubicin
AUTHOR(S): Patterson, Laurence H.; Gandecha, Bijukumar M.; Brown, Jeffrey R.
CORPORATE SOURCE: Sch. Pharm., Leicester Polytech., Leicester, LE1 9BH, UK
SOURCE: Biochemical and Biophysical Research Communications (1983), 110(2), 399-405
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB daunorubicin [20830-81-3] Administration to mice produced a marked stimulation of lipid peroxidn. in both liver and heart 48 h following administration. In contrast, 1,4-bis{2-[(2-hydroxyethyl)amino]ethylamino}-9,10-anthracenedione (HAQ)(I) [64862-96-0] did not induce lipid peroxidn. in the liver and actually inhibits it in the heart. In addition, neither daunorubicin nor HAQ depleted reduced glutathione [70-18-8] in the liver or heart 48 h after drug administration. Daunorubicin-induced glutathione depletion was observed 2.5 h following administration. These results correlate with daunorubicin increased microsomal O consumption, while HAQ produced no measurable effect on the rate of microsomal O utilization. Apparently, redox cycling to produce free radical O involved in lipid peroxidn. and glutathione depletion, an established action of daunorubicin, does not occur with HAQ. This apparent lack of HAQ reactivity may help explain the relatively low cardiotoxicity of this novel antitumor agent.

Structures uploaded into STN REGISTRY

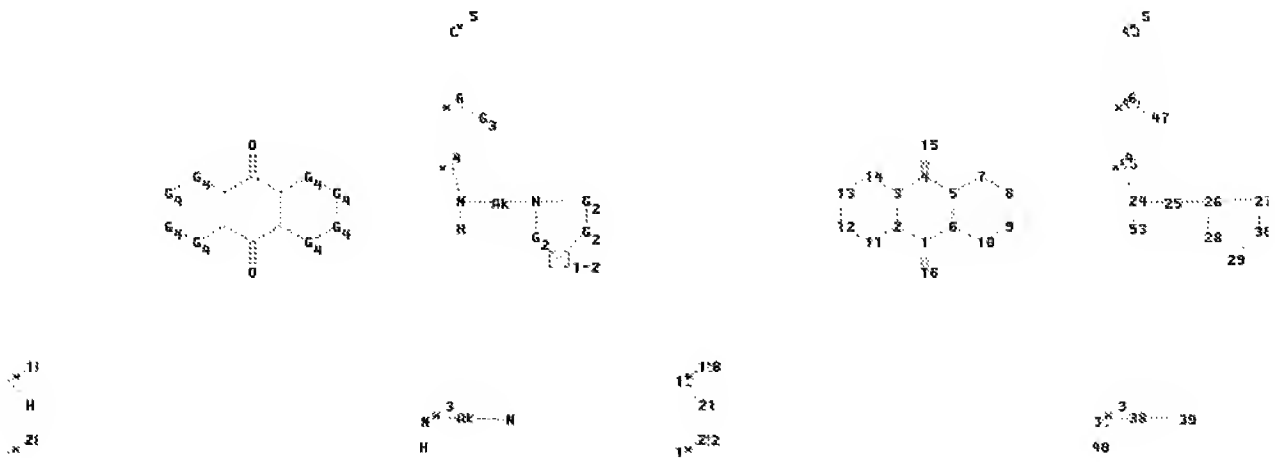
Uploading L1b.str



chain nodes :
15 16 17 18
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 19 20 21 22 23
chain bonds :
1-16 4-15 17-18 18-19
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 5-11 6-14 7-8 8-9 9-10 11-12 12-13
13-14 19-20 19-22 20-21 21-23 22-23
exact/norm bonds :
1-2 1-6 1-16 2-3 2-7 3-4 3-10 4-5 4-15 5-6 5-11 6-14 7-8 8-9 9-10
11-12 12-13 13-14 17-18 18-19 19-20 19-22 20-21 21-23 22-23

Connectivity :
15:1 E exact RC ring/chain 16:1 E exact RC ring/chain
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:Atom
20:Atom 21:Atom
22:Atom 23:Atom 27:CLASS

Uploading L10b.str



```
chain nodes :
15  16  18  19  20  21  22  23  24  25  37  38  39  40  43  44  45  47  53
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  26  27  28  29  30
chain bonds :
1-16  4-15  18-20  18-21  19-22  19-23  24-25  24-45  24-53  25-26  37-38  37-40
38-39  44-47
ring bonds :
1-2  1-6  2-3  2-11  3-4  3-14  4-5  5-6  5-7  6-10  7-8  8-9  9-10  11-12  12-13
13-14  26-27  26-28  27-30  28-29  29-30
exact/norm bonds :
1-2  1-6  1-16  2-3  2-11  3-4  3-14  4-5  4-15  5-6  5-7  6-10  7-8  8-9  9-10
11-12  12-13  13-14  18-20  18-21  19-22  19-23  24-25  24-45  24-53  25-26  26-27
26-28  28-29  29-30
37-38  37-40  38-39  44-47
exact bonds :
27-30
isolated ring systems :
containing 26 :


G1:O,X,Ak

G2:[*1],[*2]

G3:O,X,Ak,[*3]

G4:[*4],[*5],[*6]

Connectivity :
25:2 E exact RC ring/chain  38:2 E exact RC ring/chain  43:2 E exact RC ring/chain
44:3 E exact RC ring/chain  45:3 E exact RC ring/chain
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:CLASS  16:CLASS  18:CLASS  19:CLASS
20:CLASS  21:CLASS  22:CLASS
23:CLASS  24:CLASS  25:CLASS  26:Atom  27:Atom  28:Atom  29:Atom  30:Atom  37:CLASS
38:CLASS
39:CLASS  40:CLASS  43:CLASS  44:CLASS  45:CLASS  47:CLASS  53:CLASS
```

Full search history

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=> d his full

     (FILE 'HOME' ENTERED AT 13:11:47 ON 27 AUG 2008)

     FILE 'REGISTRY' ENTERED AT 13:12:40 ON 27 AUG 2008
                ACT CHA783L14ST/A
               ---------
L1              STR
L2           407 SEA SSS FUL L1
               ---------
L3              STRUCTURE UPLOADED
                D L3
L4            10 SEA SUB=L2 SSS SAM L3
                D SCAN
L5              STRUCTURE UPLOADED
                D L5
L6             9 SEA SUB=L2 SSS SAM L5
                D SCAN
L7              STRUCTURE UPLOADED
                D L7
L8            10 SEA SUB=L2 SSS SAM L7
L9             9 SEA SUB=L2 SSS SAM (L5 AND L7)
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 13:26:17 ON 27 AUG 2008

     FILE 'REGISTRY' ENTERED AT 13:35:47 ON 27 AUG 2008
L10             STRUCTURE UPLOADED
                D L10
L11            4 SEA SUB=L2 SSS SAM L10
                D SCAN
L12             STRUCTURE UPLOADED
                D L12
L13            4 SEA SUB=L2 SSS SAM L12
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 13:39:41 ON 27 AUG 2008

     FILE 'REGISTRY' ENTERED AT 13:59:09 ON 27 AUG 2008
L14           84 SEA SUB=L2 SSS FUL L10

     FILE 'HCAPLUS' ENTERED AT 14:02:38 ON 27 AUG 2008
L15           34 SEA ABB=ON  PLU=ON  L14

     FILE 'REGISTRY' ENTERED AT 14:03:28 ON 27 AUG 2008

     FILE 'HCAPLUS' ENTERED AT 14:07:35 ON 27 AUG 2008
                E PATTERSON L?/AU
L16          381 SEA ABB=ON  PLU=ON  PATTERSON L?/AU
                E PORS K?/AU
L17           13 SEA ABB=ON  PLU=ON  PORS K?/AU
                E TEESDALE-SPITTLE?/AU
                E "TEESDALE-SPITTLE"/AU
                E TEESDALE P?/AU
L18           36 SEA ABB=ON  PLU=ON  ("TEESDALE SPITTLE P"/AU OR "TEESDALE
                SPITTLE P H"/AU OR "TEESDALE SPITTLE PAUL"/AU OR "TEESDALE
                SPITTLE PAUL H"/AU OR "TEESDALE SPITTLE PAUL HENRY"/AU)
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L19           5 SEA ABB=ON  PLU=ON  L16 AND L17 AND L18
L20         407 SEA ABB=ON  PLU=ON  (L16 OR L17 OR L18)
L21           2 SEA ABB=ON  PLU=ON  L20 AND SOMANTA?/CO,CS,PA,SO
L22          18 SEA ABB=ON  PLU=ON  L16 AND (L17 OR L18)
L23           5 SEA ABB=ON  PLU=ON  L17 AND L18
L24          51 SEA ABB=ON  PLU=ON  L20 AND ?ANTHRA?
L25          47 SEA ABB=ON  PLU=ON  L20 AND ?QUINON?
L26          38 SEA ABB=ON  PLU=ON  L24 AND L25
L27          18 SEA ABB=ON  PLU=ON  L19 OR L21 OR L22 OR L23
L28          43 SEA ABB=ON  PLU=ON  L27 OR L26
L29          36 SEA ABB=ON  PLU=ON  (L24 OR L25) AND (CANCER? OR TUMOR? OR
                TUMOUR? OR CARCIN? OR NEOTOM? OR NEOPLAS?)
L30          55 SEA ABB=ON  PLU=ON  L28 OR L29
L31           8 SEA ABB=ON  PLU=ON  L30 AND (?PYRROL? OR ?PIPERIDIN?)
                D L31 1-8 TI
                D L31 1-8 AU
L32          44 SEA ABB=ON  PLU=ON  (L24 OR L25) AND (?CANCER? OR ?TUMOR? OR
                ?TUMOUR? OR ?CARCIN? OR ?NEOTOM? OR ?NEOPLAS? OR ?TOMA?)
L33          57 SEA ABB=ON  PLU=ON  L28 OR L32
L34           8 SEA ABB=ON  PLU=ON  L33 AND (?PYRROL? OR ?PIPERIDIN?)
L35          57 SEA ABB=ON  PLU=ON  L33 OR L34
                SAVE TEMP L15 CHA783HCST/A
                SAVE TEMP L35 CHA783HCIN/A

     FILE 'STNGUIDE' ENTERED AT 14:25:24 ON 27 AUG 2008

     FILE 'REGISTRY' ENTERED AT 14:50:21 ON 27 AUG 2008

     FILE 'HCAPLUS' ENTERED AT 14:50:24 ON 27 AUG 2008
                D STAT QUERY L15
                D L15 1-34 IBIB ED ABS HITSTR
                D QUE L35
                D L35 1-57 IBIB AB


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   26 AUG 2008  HIGHEST RN 1043895-06-2
     DICTIONARY FILE UPDATES:  26 AUG 2008  HIGHEST RN 1043895-06-2

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

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       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

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     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/support/stngen/stndoc/properties.html

     FILE STNGUIDE
     FILE CONTAINS CURRENT INFORMATION.
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LAST RELOADED: Aug 22, 2008 (20080822/UP).

FILE HCAPLUS

FILE COVERS 1907 - 27 Aug 2008 VOL 149 ISS 9
FILE LAST UPDATED: 26 Aug 2008 (20080826/ED)

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

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This file contains CAS Registry Numbers for easy and accurate substance identification.